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Office on Smoking and Health

1984-1985
DIRECTORY
On-Going Research in Smoking and Health

COMPLETE
347.

Office on Smoking and Health

1984-1985

DIRECTORY

On-Going Research in Smoking and Health

WORLD HEALTH ORGANIZATION
COLLABORATING CENTRE
FOR REFERENCE ON
SMOKING AND HEALTH

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CONTENTS

Page

Acknowledgements ii

Abbreviations Used for Sponsoring Organizations iii

Introduction iv

How to Use This Directory ix

Research Descriptions:

- Argentina 1
- Australia 2
- Austria 16
- Bangladesh 17
- Barbados 17
- Belgium 18
- Brazil 20
- Canada 20
- Chile 45
- China 46
- Colombia 48
- Czechoslovakia 48
- Denmark 50
- Egypt 54
- Federal Republic of Germany 55
- Finland 60
- France 68
- Greece 79
- Hong Kong 81
- Hungary 82
- India 83
- Ireland 92
- Israel 95
- Italy 99
- Japan 108
- Malaysia 120
- Nepal 121
- Netherlands 121
- New Zealand 124
- Nigeria 125
- Norway 126
- Pakistan 131
- Poland 132
- Portugal 136
- Republic of Korea 136
- Romania 137
- South Africa 138
- Sudan 139
- Sweden 139
- Switzerland 148
- Tahiti 154
- Thailand 154
- Turkey 154
- Union of Soviet Socialist Republics 155
- United Kingdom 156
- United States 186
- Zambia 509

Appendix 511

Indexes:

- Index of Principal Investigators 523
- Index of Organizations 537
- Index of Sponsors 547
- Subject Index 555

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ABBREVIATIONS USED FOR SPONSORING ORGANIZATIONS

ACS: American Cancer Society
ADAMHA: Alcohol, Drug Abuse, and Mental Health Administration
AHA: American Heart Association
ALA: American Lung Association
ATRF: American Tobacco Research Foundation
AMA: American Medical Association
ARS: Agricultural Research Service
CDC: Centers for Disease Control
CNRS: Centre National de la Rechereche Scientifique
CTR: Council for Tobacco Research - U.S.A., Inc.
DHHS: U.S. Department of Health and Human Services
DOD: U.S. Department of Defense
DOE: U.S. Department of Energy
EPA: U.S. Environmental Protection Agency
ERS: USDA, Economic Research Service
FDA: U.S. Food and Drug Administration
FTC: U.S. Federal Trade Commission
HRSA: Health Resources and Services Administration
HWC: Health and Welfare Canada
INSERM: Institut National de la Sante et de la Recherche Medicale (National Institute of Health and Medical Research)
JTSPC: Japan Tobacco and Salt Public Corporation
KTHRI: Kentucky Tobacco and Health Research Institute
KTRB: Kentucky Tobacco Research Board
MRC: Medical Research Council
NCHS: National Center for Health Statistics
NCHSR: National Center for Health Services Research
NCI: National Cancer Institute
NEI: National Eye Institute
NHLBI: National Heart, Lung, and Blood Institute
NHMRCA: National Health and Medical Research Council of Australia
NIA: National Institute on Aging
NIAAA: National Institute on Alcohol Abuse and Alcoholism
NIAID: National Institute of Allergic and Infectious Diseases
NIAMDD: National Institute of Arthritis, Metabolism, and Digestive Diseases
NICHD: National Institute of Child Health and Human Development
NIDA: National Institute on Drug Abuse
NIDR: National Institute of Dental Research
NIEHS: National Institute of Environmental Health Sciences
NIGMS: National Institute of General Medical Sciences
NIH: National Institutes of Health
NIMH: National Institute of Mental Health
NIOSH: National Institute for Occupational Safety and Health
NINCDS: National Institute of Neurological and Communicative Disorders and Stroke
NRC: Nuclear Regulatory Commission
NSF: National Science Foundation
ORNL: Oak Ridge National Laboratory
OSH: Office on Smoking and Health
USPHS: Public Health Service
UICC: Union Internationale Contre le Cancer (International Union Against Cancer)
USA: U.S. Army
USAF: U.S. Air Force
USDA: U.S. Department of Agriculture
USUHS: Uniformed Services University of the Health Sciences
VA: U.S. Veterans Administration
WHO: World Health Organization

Introduction

The *Directory of On-going Research in Smoking and Health* is a compilation of current, on-going research being conducted throughout the world on smoking, tobacco, and tobacco use. This tenth edition of the *Directory* contains approximately 1,600 projects from 49 countries. Projects were received from an additional ten countries that were not represented in the 1982 *Directory*. The total number of projects represents a 45 percent increase over the number included in 1982.

Method of Data Collection

The Technical Information Center (TIC) of the Office on Smoking and Health, which has direct responsibility for compiling the *Directory*, accomplishes the task in several ways:

1. A master mailing list is developed by the TIC, which has a contract with an information science group that systematically monitors the scientific literature. Names, addresses, and institutional affiliations of potential researchers are identified and used to create a core master mailing list.

2. All investigators whose projects were included in the previous *Directory* are automatically included in the master list.

3. Searches are made against numerous automated data bases available within and outside government for names of additional researchers. The Computer Retrieval of Information on Scientific Projects (CRISP) system of the National Institutes of Health and the Current Research Information System (CRIS) of the U.S. Department of Agriculture are examples of the larger data bases that are searched.

4. Requests are sent to institutions that conduct tobacco-related research and lists of investigators from these sources are incorporated into the master mailing list. Two of the largest institutions, the University of Kentucky Tobacco and Health Research Institute and the Council for Tobacco Research, U.S.A., Inc., routinely send lists of their grantees.

5. A cover letter, explaining the purpose of the *Directory*, and two questionnaires are sent to each investigator on the master mailing list. Investigators are requested to complete a separate questionnaire for each project related to smoking and health in which they are involved. If a summary of an investigator's project is available, either from a computer data base or from the previous *Directory*, a copy is included to assist the investigator in updating or modifying the project description.

6. At the end of 4 weeks, a followup letter is sent (with another copy of the questionnaire) to those investigators who did not respond to the initial mailing. Additional time (approximately 2 weeks) is allowed for returns from non-U.S. sources. A final followup letter is mailed 4 weeks later.

7. In some instances, further communication is necessary to clarify any ambiguities and to ensure that all project descriptions are as complete as possible. A project description is included in the *Directory* when a signed and completed form is returned by the investigator. However, in a few cases where a project summary is located in a Federally supported data base and is considered to be in scope, and the investigator does not respond, the summary from the original data base source is included in the *Directory*.

Analysis of Research Summaries

An analysis was performed for only the 1,563 projects for which complete descriptions were available at the time the *Directory* went to press. Another 48 projects, listed by country in the Appendix, were received too lated to be fully processed. Because projects are included only if questionnaires are received from investigators, the *Directory* should not be considered all inclusive. That is, some investigators did not respond or the Office did not know of the existence of a particular project when the master mailing list was compiled. In a few cases, project summaries were not included because the scope of the research was not considered to conform to *Directory* requirements.

The United States contributed well over half of the 1563 projects (63 percent) with 960 descriptions, an increase of more than 41 percent over the 565 projects in the 1982 *Directory*. Many involved investigations in the area of direct biomedical research (233 projects) such as the association of smoking or tobacco use with specific diseases or studies examining the chemistry of tobacco smoke and its individual constituents on the mechanism of disease production. However, a significant number were also devoted to the behavioral and psychological aspects of smoking (195 projects) including why people smoke, the possible role of nicotine in the maintenance of the habit, and ways to successfully intervene with smoking behavior.

Table 1 presents a detailed analysis by country and major subject category for the 1,563 projects listed in the 1984-1985 *Directory*. Each project is catalogued only once by what was judged to be the primary area of research; however, a significant number involved several research areas.

Following the United States, the next largest number of projects (98) was received from the United Kingdom (England, Scotland, and Wales), followed by Canada (78), Australia (46), Japan (43), France (34), Italy (32), India (31), Sweden (29), and Finland (25). Each of the remaining 37 countries contributed fewer than 20 projects.

There are several reasons for the identification of an ever increasing number of research projects on smoking and health:

1. The methods used to identify researchers has been improved and expanded;

2. followup and tracking procedures are more efficient and we are thus able to obtain a greater number of completed responses; and

3. the definition of smoking and health research now includes projects in which smoking was not the primary focus of the research, but in which relevant data on smoking was collected.

We expect that this trend will continue and that the next edition of the *Directory* will include an even greater number of projects.

Federal Role in Smoking Research

As might be expected, a large number of research projects related to smoking were sponsored or supported by the Federal government. A total of 685 projects were identified that receive whole or partial support from a Federal agency.

The U.S. Department of Agriculture's tobacco research program provided support for 66 projects involving smoking and health. However, the Federal agency most involved in smoking and health research is the U.S. Department of Health and Human Services, particularly agencies within the Public Health Service such as the various institutes of the National Institutes of Health. The Department of Health and Human Services supports 474 of the research projects included in the

1984-1985 *Directory*, of which 347 are within the National Institutes of Health. The majority of these (265) are supported by the two largest institutes; the National Cancer Institute (158 projects) and the National Heart, Lung, and Blood Institute (107 projects).

Other Federal agencies that support smoking and health research are the Department of Defense (8 projects), Veterans Administration (119 projects), Environmental Protection Agency (14 projects), and the Department of Energy (4 projects). Table 2 provides information on the number of projects supported or sponsored by Federal health agencies within the Department of Health and Human Services.

TABLE 1

Smoking and Health Research, by Country and Major Subject Category

COUNTRY	1984-1985 CATEGORIES* A	B	C	D	E	F	G	H	I	J	K	L
Argentina (2)	0	1	0	0	0	0	0	1	0	0	0	0
Australia (46)	0	2	6	2	6	2	2	9	6	9	0	2
Austria (2)	0	0	1	0	1	0	0	0	0	0	0	0
Bangladesh (2)	0	0	1	0	0	0	0	1	0	0	0	0
Barbados (1)	0	0	0	0	0	0	0	0	0	0	1	0
Belgium (6)	0	1	0	3	0	0	1	1	0	0	0	0
Brazil (1)	0	0	0	1	0	0	0	0	0	0	0	0
Canada (78)	0	10	8	3	13	7	3	8	13	6	2	5
Chile (3)	0	0	0	0	0	0	3	0	0	0	0	0
Colombia (1)	0	0	1	0	0	0	0	0	0	0	0	0
Czechoslovakia (5)	0	1	0	3	1	0	0	0	0	0	0	0
Denmark (17)	0	4	3	2	2	3	3	0	0	0	0	0
Egypt (1)	0	0	0	0	0	0	0	1	0	0	0	0
Fed. Rep. of Germany (18)	0	7	4	1	3	1	0	0	2	0	0	0
Finland (25)	0	8	0	4	0	4	0	3	2	2	1	1
France (34)	0	6	6	1	8	2	5	2	1	3	0	0
Greece (6)	0	0	2	1	1	0	0	1	0	1	0	0
Hong Kong (3)	0	0	3	0	0	0	0	0	0	0	0	0
Hungary (3)	0	0	2	0	0	0	1	0	0	0	0	0
India (31)	0	6	6	3	8	0	1	1	0	2	4	0
Ireland (10)	0	0	1	6	1	0	0	2	0	0	0	0
Israel (13)	0	0	1	1	0	0	2	3	1	4	1	0
Italy (32)	0	5	12	1	4	1	0	3	2	3	0	1
Japan (43)	0	15	6	1	6	2	5	3	0	0	1	4
Malaysia (1)	0	1	0	0	0	0	0	0	0	0	0	0
Nepal (1)	0	0	0	0	0	0	1	0	0	0	0	0
Netherlands (9)	0	3	1	1	0	0	0	2	0	2	0	0
New Zealand (3)	0	0	0	1	0	0	0	1	0	0	0	1
Nigeria (1)	0	0	0	0	0	0	0	1	0	0	0	0
Norway (17)	0	2	1	3	1	3	0	6	0	0	1	0
Pakistan (2)	0	0	1	0	0	0	1	0	0	0	0	0
People's Rep. of China (8)	0	0	2	2	0	0	0	3	0	0	1	0
Poland (13)	0	3	2	1	4	0	3	0	0	0	0	0
Portugal (2)	0	1	0	0	0	0	0	0	0	0	0	1
Puerto Rico (1)	0	0	0	1	0	0	0	0	0	0	0	0
Republic of Korea (3)	0	2	0	0	0	0	0	0	0	0	0	1
Romania (1)	0	0	1	0	0	0	0	0	0	0	0	0
South Africa (3)	0	0	2	0	0	0	0	1	0	0	0	0
Sudan (1)	0	0	0	0	0	0	0	1	0	0	0	0
Sweden (29)	0	4	5	4	4	2	6	0	2	0	1	1
Switzerland (19)	0	3	2	0	3	0	2	7	2	0	0	0
Tahiti (1)	0	0	0	0	1	0	0	0	0	0	0	0
Thailand (1)	0	1	0	0	0	0	0	0	0	0	0	0
Turkey (2)	0	2	0	0	0	0	0	0	0	0	0	0
Union of Sov. Soc. Rep. (3)	0	0	0	1	0	0	0	1	0	1	0	0
United Kingdom												
England (76)	0	9	4	7	8	3	5	19	6	9	5	1
Scotland (13)	0	3	1	2	1	0	2	1	1	1	1	0
Wales (10)	0	1	0	1	0	0	1	2	3	1	0	1
Zambia (1)	0	0	0	0	0	0	0	1	0	0	0	0
United States (960)	23	233	107	77	76	44	50	119	106	77	21	27

*A - Agriculture; B - Chemistry, Pharmacology and Toxicology; C - Cancer; D - Cardiovascular Disease; E - Lung Disease; F - Pregnancy and Infant Health; G - Other Diseases and Conditions; H - Behavioral and Psychological; I - Cessation; J - Prevention/Intervention; K - Overall Mortality and Morbidity; L - General

TABLE 2

Smoking and Health Related Research

Of the U.S. Public Health Service

Agency	Number of Projects
Office of the Assistant Secretary for Health	9
Office on Smoking and Health	5
National Center for Health Services Research	2
Alcohol, Drug Abuse, & Mental Health Administration	2
National Institute on Alcohol Abuse and Alcoholism	13
National Institute on Drug Abuse	59
National Institute of Mental Health	10
Centers for Disease Control	8
National Institute for Occupational Safety and Health	11
Food and Drug Administration	6
Health Resources and Services Administration	2
National Institutes of Health	25
National Cancer Institute	158
National Eye Institute	1
National Heart, Lung, and Blood Institute	107
National Institute on Aging	4
National Institute of Allergy and Infectious Diseases	3
National Institute of Arthritis, Metabolism and Digestive Diseases	7
National Institute of Child Health and Human Development	31
National Institute of Dental Research	1
National Institute of Environmental Health Sciences	6
National Institute of General Medical Sciences	3
National Institute of Neurological and Communicative Disorders and Stroke	1
Total Department of Health and Human Services	474

HOW TO USE THIS DIRECTORY

Research resumes in the *Directory* are arranged in alphabetical order by country, and within each country, alphabetically by institution. In the United States section, resumes are in alphabetical order by state, and in the United Kingdom section, in order by country (i.e., England, Scotland, and Wales).

Four indexes – Principal Investigator, Subject, Sponsor, and Organization – provide easy access to information in the *Directory*. Numbers in all indexes refer to resume numbers rather than page numbers.

Information in the project descriptions is as complete as possible, although a limited amount of editing has been done to clarify ideas or to condense particularly long resumes. Missing items in the description indicate omissions in the report furnished to the Office on Smoking and Health.

The Appendix included at the end of the research resumes provides a listing of reports received too late to be completely processed. These projects are referenced in the Index of Principal Investigators only.

1984-1985 DIRECTORY OF ON-GOING RESEARCH IN SMOKING AND HEALTH

ARGENTINA

0001. CENTRO DE INVESTIGACIONES TOXICOLOGICAS, CITEFA/CONICET, Zufriategui 4380, 1603 Villa Martelli, Pcia, Buenos Aires, Argentina.

Project Title:
Nitrosamines and Tobacco Smoke.

Principal Investigators:
Castro, J.A.; Diaz Gomez, M.I.

Objective:
To establish potential risks from smoking attributable to the presence of nitrosamines in tobacco smoke.

Methods or Approach:
^{14}C-nitrosamines present in tobacco smoke (NDMA, N-PYR, or NNN) are given to nursing rats; after 24 hours of breast milk feeding, sucklings are sacrificed. Livers and kidneys of sucklings are removed and DNA and RNA are isolated, purified, and counted for covalently bound label. Isolation followed by hydrolysis and column chromatography establishes formation of N$_7$ and O$_6$ methylated bases of DNA after NDMA administration.

Results to Date:
Administration of ^{14}C-NDMA, N-PYR, or NNN to nursing female rats led to transmission of covalently bound ^{14}C to liver and kidney DNA and RNA of sucklings. When ^{14}C-NDMA is given to nursing rats, liver DNA from sucklings contains N$_7$ and O$_6$ bases. Results suggest risks for breastfed babies whose mothers are smokers.

Future Plans:
Attempts will be made to determine whether NDMA, N-PYR, and NNN are metabolized and activated in ovaries to form reactive metabolites covalently binding to their DNA and RNA, and whether N$_7$ and O$_6$ methylated bases are formed after NDMA administration.

Project Dates:
January 1984–April 1985.

Financial Support:
Centro de Investigaciones Toxicologicas, Argentina; National Council for Research, Argentina.

0002. ESCUELA NACIONAL DE EDUCACION TECNICA NO. 5, 9 de Julio 772, 5500 Mendoza, Argentina.

Project Title:
Attitudes of Teachers and Students Toward Smoking at National Technical Education School.

Principal Investigator:
Baragiola, A.M.

Objective:
To determine attitudes toward smoking among teachers and students using three tests originally used by Horn.

Methods or Approach:
Test No. 3 was used in June 1984; tests 1 and 2 will be used in phase II of the survey. With teenage students, however, a translated form of the "Teenage Cigarette Smoking Self-Test and Discussion Leader's Guide" will be used. Results will be correlated.

Results to Date:
Preliminary findings, published in local newspapers, show reasons for smoking were relaxation, 11.04 percent; as a crutch, 10.01 percent; craving, 7.41 percent; handling, 7.06 percent; stimulation, 5.93 percent; and habit, 5.25 percent. Average age of students was 23.76 years; mean length of smoking was 7.16 years; mean consumption, 12.61 cigarettes/day. Blond cigarettes were the most popular (59 percent), followed by dark tobacco cigarettes (29 percent), blond/dark (3 percent). Nine percent did not specify type smoked. Most smokers reported having family members who smoked (76 percent); 15 reported no family smokers; 9 percent did not specify. When asked if they had considered quitting, 77 percent answered yes, 10 percent no, and 13 percent did not reply. It is hoped that since the tests will be familiar to students (particularly those in the postgraduate course on occupational safety and health), they will be used for research and as prevention tools at worksites.

Project Dates:
June 1984–1986.

0003. ANTI-CANCER COUNCIL OF VICTORIA, 90 Jolimont Street, East Melbourne, Victoria 3002, Australia.

Project Title:
UICC Special Project on Smoking and Cancer.

Principal Investigator:
Gray, N.J.
Objective:
To (1) assist members of the International Union Against Cancer (UICC), cancer leagues, and societies in drawing up a model strategy for smoking control programs covering the areas of legislation, information, education, and cessation; (2) help adapt the model strategies to local conditions; and (3) provide advice on ways of implementation by organizing regional workshops.
Methods or Approach:
On the basis of a model program, the UICC organizes regional workshops/seminars to analyze local problems, assess local potential preventive action, help develop techniques for delivery of programs appropriate to the region, and help in the establishment of priority targets for public information and education, legislation, and regional policy development.
Results to Date:
The document entitled *Lung Cancer Prevention–Guidelines for Smoking Control* was published, and 2,000 copies were distributed throughout the world. An updated second edition entitled *Guidelines for Smoking Control,* UICC Technical Report Series Vol. 52, Geneva 1980, has also been published. A team of consultants has been formed, and workshops have been organized in Manila, London, Buenos Aires, Sao Paulo, Porto Alegre, Rio de Janeiro, Cairo, Bombay, Paris, Kuwait, Colombo, Singapore, Lagos, and Nagoya. In addition, Spanish and German editions of the manual have been published.
A manual entitled *Children and Smoking* has been published, as has a manual on smoking cessation techniques, in addition to the continuation of workshop programs.
Project Dates:
1966–continuing.
Financial Support:
UICC–NORAD.

0004. ANTI-CANCER COUNCIL OF VICTORIA, 90 Jolimont Street, East Melbourne 3002, Australia.

Project Title:
Patterns of Tobacco Smoking in Australia.

Principal Investigators:
Gray, N.J.; Hill, D.J.
Objective:
To determine smoking behavior and related beliefs and intentions in Australia.
Methods or Approach:
A nationwide household survey of 5,580 men and women, aged 16 and over, was conducted in 1983.
Results to Date:
Among males, 37 percent were regular cigarette smokers (a significant drop from 40 percent reported in 1980). Among females, 30 percent were smokers compared with 31 percent in 1980. In those aged 16 to 24, more females than males smoked cigarettes and there was evidence of a net increase in smoking among females at about age 50. Male smokers had stronger intentions to give up than female smokers. The main advantages of giving up listed by ex-smokers were health-related and the main disadvantages were weight gain and irritability. Current smokers also listed advantages in giving up, but they were more likely to list weight gain and irritability as disadvantages. Only 8 percent of smokers listed their own doctor among the people who would be in favor of them quitting. More nonsmokers than smokers listed diseases caused by smoking and 25 percent of smokers (9 percent of never smokers) believed no illnesses are caused by smoking. Among smokers, a highly significant positive relationship was found between the belief that one's own smoking could cause a fatal illness and the intention to quit.
Financial Support:
Australian Government.

0005. ANTI-CANCER COUNCIL OF VICTORIA, 1 Rathdowne Street, Carlton South, Victoria 3053, Australia.

Project Title:
Secondary School Smoking Survey.

Principal Investigators:
Hill, D.J.; Willcox, S.; Gardner, G.J.
Objective:
To measure prevalence of tobacco and alcohol use in Australian secondary school students.
Methods or Approach:
A representative sample of more than 20,000 students was drawn from schools in all States of Australia. An anonymous survey questionnaire was administered by trained visiting research assistants to groups (approximately 20 students randomly sampled from school rolls, i.e., nonintact classes). Past and current smoking and drinking behavior, intentions, self-referent labels, and cigarette brand usage were determined.
Results to Date:
Data collection has been completed, but results are not yet available.
Future Plans:
The survey will be repeated periodically to monitor secular and geographic trends.
Project Dates:
October 1983–June 1985.
Financial Support:
Anti-Cancer Council of Victoria; State Government of Victoria.

0006. AUSTRALIAN COUNCIL ON SMOKING AND HEALTH, 705 Murray Street, West Perth, Western Australia 6005, Australia.

Project Title:
Secondary School Smoking Survey.

Principal Investigators:
Shean, R.E.; Clark, K.
Objective:
To establish smoking prevalence rates among adolescents in Western Australian primary and secondary schools; determine smoking prevalence trends within the State to allow for evaluation of the State government's "Smoking Prevention Programme for Primary Schools."
Methods or Approach:
As part of a national survey on smoking prevalence, responses

on cigarette smoking and alcohol consumption were elicited by a 23-item questionnaire administered in August 1984. The sample consisted of 3,028 students in years 7 through 12 (12 to 17 years of age) in 65 government and non-government primary and secondary schools in both rural and metropolitan areas. Within each school, students were selected at random from class lists. Responses from 3,020 students were analyzed.

Results to Date:

Smoking rates for adolescents are unacceptably high, with prevalence rates among 15-year-olds who smoke regularly approaching those of adult smokers. In years 7 and 8, however, there has been a substantial decline in prevalence rates since 1983. It is noted that the prevention program was introduced in year 7 of all primary schools in the State in September 1983. Increased teacher awareness of smoking control through inservice training, the prevention program for students, and the Health Department of Western Australia's antismoking media campaign may well be responsible for the decline.

Future Plans:

Subsequent analysis will focus on acquisition of smoking among adolescents; in particular, the relative percentage of current experimental and regular smokers will be investigated.

Project Dates:

March 1984–December 1985.

Financial Support:

Western Australian Alcohol and Drug Authority; Cancer Foundation of Western Australia.

0007. AUSTRALIAN GOVERNMENT ANALYTICAL LABORATORIES, 13th Floor, 11 William Street, Melbourne, Victoria 3000, Australia.

Project Title:

Smoking and Health.

Principal Investigator:

Jephcott, R.W.

Objective:

To provide and publish a public list of tar, nicotine, and carbon monoxide yields from all local and imported brands of cigarettes marketed in Australia.

Methods or Approach:

Testing of locally manufactured and imported cigarette brands has been carried out regularly since 1975. For local brands, samples are taken at point of manufacture. Gas chromatographic techniques are used for determination of water and nicotine; a nondispersive infrared method is employed for measurement of carbon monoxide. Tar is obtained by subtraction of water and nicotine from total extract.

Results to Date:

Results from the latest survey show the following ranges for domestic cigarettes: tar, from 1 to 15 mg/cigarette; nicotine, 0.1 to 1.3 mg/cigarette; and carbon monoxide, from 2 to 16 mg/cigarette. Values for imported cigarettes are 1 to 29 mg tar/cigarette, 0.2 to 1.7 mg nicotine, and from 2 to 25 mg carbon monoxide/cigarette.

Future Plans:

Surveys will continue to be conducted every 2 years.

Project Dates:

July 1975–continuing.

Financial Support:

Australian Government.

0008. BUSSELTON HEALTH CENTRE, UNIVERSITY OF WESTERN AUSTRALIA, Raine Medical Statistics Unit, Nedlands, Western Australia 6009, Australia.

Project Title:

Alcohol, Tobacco and Analgesics–Busselton 1972.

Principal Investigators:

Cullen, K.J.; Stenhouse, N.S.

Objective:

To discuss the consumption of alcohol, tobacco, and analgesics among Busselton adults; compare patterns with the population in a North Shore suburb of Sydney.

Methods or Approach:

Subjects completed a self-administered questionnaire including the following questions on smoking: "Which of the following best describes your smoking habits? nonsmoker, ex-smoker, cigarette smoker, pipe smoker, cigar smoker"; "If you are a cigarette smoker do you smoke less than 15 cigarettes per day, more than 15 cigarettes per day?" "If applicable, age started."

Results to Date:

The prevalence of smoking among men decreased from 53 percent in 1966 to 44 percent in 1972, women showing no significant change (24 percent). The age at which various age groups start smoking would suggest that more young women are smoking and more are starting to smoke at earlier ages. Young men tended to take up smoking at earlier ages, but as a group they appear to contain a higher proportion of nonsmokers than do older age groups. The prevalence of male nonsmokers decreases and female nonsmokers increases with increase in age. Young people have been starting to smoke at a younger age than did their elders. Comparisons with a North Shore suburb of Sydney indicate that more Busselton people (particularly women) abstained from tobacco.

Project Dates:

November 1972–continuing.

Financial Support:

Arnold Yeldham and Mary Raine Research Foundation; Royal Perth Hospital Research Fund; National Health and Medical Research Council; University of Western Australia; National Heart Foundation; Western Australia Telethon.

0009. COMMONWEALTH INSTITUTE OF HEALTH, UNIVERSITY OF SYDNEY, New South Wales 2006, Australia.

Project Title:

Sydney "Quit For Life" Evaluation.

Principal Investigators:

Dwyer, T.; Pierce, J.P.

Objective:

To design and implement an integrated antismoking campaign using all available methods of influence and thus reduce the prevalence of smoking in the Sydney area.

Methods or Approach:

Specific aims were to (1) use advertising in the mass media and by direct mail to convince people that now is a good time to quit smoking; (2) generate an indepth discussion in the general mass media about the importance of and difficulties in quitting, current recommended strategies for quitting, and other aspects of smoking; (3) coordinate, recommend, and actively promote an advising and helping role in smoking cessation among health care professionals, particularly those with large one-on-one contacts with smokers; (4) make readily available to the community the latest recommendations on how to quit smoking and actively promote this availability; (5) promote

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educational innovations that target reduction of smoking incidence among teenagers (the most successful current method emphasizes personal development through peer support programs); and (6) evaluate campaign effectiveness in reducing prevalence of smoking, increasing the number of people trying to quit, and achieving the other specific goals outlined. Surveys were conducted in April-May 1983 and April-May 1984; several telephone interviews of the Sydney sample were conducted.

Results to Date:
There has been a substantial decline, across age groups, in smoking prevalence among Australian males over the last 15 years. In recent years, the decline has been marked in those aged 20 to 24. The decline is much less marked in females; the proportion of younger women who smoke has been increasing and now, for the first time, exceeds the proportion of men of similar age who smoke. Smoking varies considerably by sociodemographic variables. Commercials had a high recall rate and considerable initial impact; however, ex-smokers and nonsmokers saw the commercials as more helpful to quitting than did smokers. During the campaign, the issue of smoking increased in salience in the community and the misconception that smokers are in the majority decreased markedly (important because the majority of people tend to change behavior towards perceived norms). There were favorable changes in the proportion of people who felt that they might quit in the short term, which were particularly marked among those who could be considered "hard core" smokers; however, there were no increases in the "extremely likely" category (thought to be the best indicator of short-term change in prevalence). The amount of self-reported discussion among friends and in social networks on the issue of smoking was less than was hoped. This variable is also thought to be a good indicator of short-term change in prevalence.

Future Plans:
Characteristics of nonrespondents will be identified and compared with those of respondents and the degree of selection bias will be estimated. This estimation will be included in overall conclusions on the generalizability of this type of campaign and the internal validity of the evaluation.

Project Dates:
May 1983–December 1984.

Financial Support:
Commonwealth Department of Health (HSD 68).

0010. HEALTH COMMISSION OF VICTORIA, 555 Collins Street, Melbourne, Victoria 3000, Australia.

Project Title:
Smoking in Hospitals - Attitudes and Practices.

Principal Investigator:
Rankin, D.W.

Objective:
To examine attitudes and practices adopted by hospitals toward smoking (worldwide if possible); determine if the situation can be considered satisfactory.

Methods or Approach:
Members of the World Health Organization's Expert Advisory Panel on Smoking and Health were asked to forward any material produced after 1975 on the subject of smoking in hospitals (attitudes and practices). The 29 countries represented on the panel were contacted.

Results to Date:
Project is in a preliminary phase.

Project Dates:
August 1984–January 1985.

Financial Support:
WHO.

0011. HEALTH COMMISSION OF VICTORIA, 555 Collins Street, Melbourne, Victoria 3000, Australia.

Project Title:
Hospital Smoking Policies in Victoria.

Principal Investigators:
Rankin, D.W ; Hill, D.J.; Stevens, K.Y.

Objective:
To determine current smoking policies in hospitals in Victoria; compare them with policies in force in 1980.

Methods or Approach:
All private, public, psychiatric, geriatric, and nursing care hospitals in Victoria having 50 beds or more (n = 171) were sent a pretested questionnaire. Information was requested on whether smoking was permitted, recent changes in smoking policies, nature of smoking restrictions, whether cigarettes were sold on the premises, and availability of hospital-based cessation programs for staff and patients. The response rate was 77 percent.

Results to Date:
Of 132 respondents, 64 percent were public hospitals; 84 percent imposed some restrictions, and in 43 percent of these, objections had been raised by patients and staff. Smoking was permitted in wards in 24 percent of acute care and 10 percent of nonacute care hospitals; in waiting areas, it was permitted in 23 percent of acute care and 9 percent of nonacute care facilities. Restrictions in dining areas were 62 percent acute care, 36 percent nonacute care; in offices, 22 and 29 percent; in patient day rooms, 44 and 50 percent; and in "all or most areas," 9 and 16 percent, respectively. A change in policy occurred in 32 percent during the past year, brought about mostly by administrative staff. Cigarettes are sold in 38 percent of acute care and 50 percent of nonacute care hospitals. Only 9 percent had cessation programs. There was no statistically significant improvement in parameters measured between current data and that from 1980 (based on identical questionnaires and methods).

Future Plans:
Data obtained will be used to promote nonsmoking in hospitals and for other smoking control programs.

Project Dates:
April 1983–August 1983.

Financial Support:
Health Commission of Victoria.

Reference:
Rankin, D.W.; Hill, D.J.; Stevens, K.Y. "Hospital Smoking Policies in Victoria." *Australian Health Review* 7(2):114-117, 1984.

0012. HEALTH DEPARTMENT OF WESTERN AUSTRALIA, HEALTH PROMOTION SERVICES, 533 Hay Street, Perth, Western Australia 6000, Australia.

Project Title:
Survey of Smoking Among Schoolchildren in Western Australia.

Principal Investigator:
Brown, H.L.

Objective:
To collect information on the prevalence of smoking among schoolchildren in Western Australia.

Methods or Approach:
The project surveyed children in the final year of primary school and the first 3 years of high school (government and independent schools in the Perth metropolitan area and in the country). A brief, anonymous questionnaire was administered in the classroom under supervision of a trained interviewer. Responses were obtained from approximately 16,000 students.
Results to Date:
Most children had experimented with cigarettes before the end of primary school; 67 percent of boys and 51 percent of girls in year 7 claimed that they had tried smoking a cigarette. Although girls began experimenting with cigarettes later than boys, the girls caught up during high school. By the end of the third year of high school, 80 percent of boys and 81 percent of girls had tried smoking. Similar trends were evident in development of regular smoking. In metropolitan schools, 23 percent of boys and 26 percent of girls usually smoked one or more cigarettes/week by the end of the third year of high school. In country schools, 24 percent of boys and 30 percent of girls were regular weekly smokers.
Future Plans:
The survey will be repeated in July/August 1985 to monitor trends in smoking among schoolchildren.
Project Dates:
July 1985–December 1985.
Financial Support:
Health Department of Western Australia.

0013. HEALTH DEPARTMENT OF WESTERN AUSTRALIA, HEALTH PROMOTION SERVICES, 533 Hay Street, Perth, Western Australia 6000, Australia.

Project Title:
Survey of Smoking Among Adults in Western Australia.

Principal Investigator:
Brown, H.L.
Objective:
To collect information on smoking habits of adults in Australia; determine attitudes toward various issues related to smoking.
Methods or Approach:
The survey sample included 4,130 households in the Perth metropolitan area and surrounding rural area. At each household, a respondent was randomly selected from usual residents aged 16 years or over. Full responses were obtained for 84.69 percent of households (nonresponse 7.6 percent, sample loss 7.8 percent). Questions were included on smoking habits, perceived importance of smoking as a community health concern, and attitudes toward restrictions on smoking in public places. Smokers were asked additional questions relating to history or previous attempts to stop smoking, desire to stop, reasons for wanting to stop, and perceived smoking-related health effects.
Results to Date:
An estimated 34.9 percent of males and 27.5 percent of females are current smokers; 32.2 percent of males and 19.0 percent of females are ex-smokers. Prevalence of smoking was highest among females aged 24 years or less (39 percent) and among males aged 25 to 29 (45 percent).
Future Plans:
The survey will be repeated in March-April 1985 to monitor changes that have occurred during the first year of a 3-year antismoking campaign for adults.
Project Dates:
February 1984–August 1985.
Financial Support:
Health Department of Western Australia.

0014. HEALTH DEPARTMENT OF WESTERN AUSTRALIA, HEALTH PROMOTION SERVICES, 533 Hay Street, Perth, Western Australia 6000, Australia.

Project Title:
Effect of Size and Position of Health Warnings in Magazine Advertisements for Cigarettes.

Principal Investigators:
Brown, H.L.; Robinson, K.
Objective:
To determine whether memory for health warnings depends on their size and position in magazine advertisements for cigarettes.
Methods or Approach:
The project used an incidental memory paradigm with accuracy of recognition as the major dependent variable. The 72 participants completed two tasks: an initial orienting task asking them to rate a series of advertisements for alcohol and cigarettes for effectiveness in "getting the message across," and a subsequent recognition memory task where they indicated whether or not particular warnings had appeared on cigarette advertisements in the preceding presentation. Health warnings were adapted from American and Swedish health education programs. Warning size was varied to take up 10 or 20 percent of page area, and warnings were located either at the top or bottom of the page. Warnings, in 28 or 14 point type, were black on a white background. Size and position were varied on a within-subjects basis. The 18 cigarette advertisements were paired with 18 health warnings, where each warning was presented in all possible combinations of size and position, and seen an equal number of times across subjects.
Results to Date:
Memory for larger warnings were significantly better than for warnings occupying only 10 percent of the page, but position on the page had no effect on whether warnings were processed and retained. The interaction of size and position was not significant.
Project Dates:
October 1984–December 1984.
Financial Support:
Health Department of Western Australia.

0015. HEALTH DEPARTMENT OF WESTERN AUSTRALIA, HEALTH PROMOTION SERVICES, Perth, Western Australia 6000, Australia.

Project Title:
Short Term Evaluation of a Mass Media Anti-Smoking Campaign for Adults.

Principal Investigators:
Donovan, R.J.; Brown, H.L.; Fisher, D.
Objective:
To assess effectiveness of an antismoking campaign designed to induce smokers to reduce consumption or stop smoking; collect information about exposure to different aspects of the campaign, use of services, and attitudes toward the campaign.
Methods or Approach:
The campaign, part of a 3-year smoking and health project, involved a media component supported by community activities and special programs for health professionals. The media component consisted of four phases, each with a different purpose and message: (1) 4-week phase designed to raise

awareness of the effects of smoking on health and increase smokers' motivation to quit; (2) 3-week phase intended to encourage smokers to make a commitment to quit; (3) 1-week phase provided support and assistance to people trying to quit through a 5-day quit program; and (4) 5-week maintenance phase. Before the campaign, a random sample of 938 smokers in the Perth metropolitan area were interviewed by telephone about smoking history and current smoking habits. Subsamples were contacted at the end of phases 1, 2, and 3, to establish whether smoking habits had changed and to assess exposure to campaign material and use of services and products. All those identified as having reduced consumption or quit smoking were reinterviewed at the end of phase 4 to determine the percentage of recidivists.

Results to Date:
Results suggest that approximately one in three smokers attempted to quit or reduce consumption during the initial 8 weeks of the campaign, and that one in six smokers quit, which represents an estimated 5 percent of smokers who quit completely and 10 percent who reduced consumption. Awareness of the campaign and the media elements was generally very high; over 90 percent of smokers reported exposure to one or more of the television commercials shown up to the end of phase 2, and 95 percent reported awareness of the 5-day quit program. Smokers expressed a high level of support for the campaign; approximately two-thirds were in favor, one-quarter were opposed, and the remainder were undecided or had no view. The level of support was sustained throughout the campaign.

Project Dates:
April 1984–September 1984.

Financial Support:
Health Department of Western Australia.

0016. NATIONAL HEART FOUNDATION OF AUSTRALIA, P.O. Box 2 Woden, Canberra A.C.T. 2606, Australia.

Project Title:
Risk Factor Prevalence Study 1980.

Principal Investigator:
Bennett, S.A.

Objective:
To (1) determine prevalence of factors thought to be associated with increased risk of cardiovascular disease in Australians aged 25 to 64 years living in State capital cities; (2) compare prevalence between geographical regions and population groups; (3) correlate prevalence with mortality from cardiovascular disease; (4) provide data that can be used as a baseline in evaluation of effectiveness of programs aimed at reducing or modifying risks; (5) provide guidelines for appropriate deployment of community resources in prevention and treatment of atherosclerotic disease; and (6) assess degree to which trends in mortality from coronary heart disease are associated with changes in prevalence of risk factors.

Methods or Approach:
A nationwide study of the prevalence of risk factors for ischemic heart disease was conducted in all Australian state capital cities. Risk factors of interest included raised blood lipid levels, raised blood pressure, cigarette smoking, overweight, physical inactivity, and psychological stress. Information was also collected on conditions and treatment, contraceptive use, use of medications, alcohol use, and dietary behavior. Background variables included age, sex, marital status, country of origin, years of Australian residence, education, employment status, and occupation. A sample of 1,200 persons was selected in the seven survey centers. Response to the 1980 survey was 76 percent.

Results to Date:
Results have been published.

Future Plans:
Results of a second survey, conducted in 1983, will be published in 1985. Future surveys are scheduled for 1988 and 1993.

Project Dates:
May 1980–November 1980.

Financial Support:
National Heart Foundation of Australia; Commonwealth Department of Health, Australia.

Reference:
National Heart Foundation of Australia. *National Heart Foundation Risk Factor Prevalence Study Report No. 1.* Canberra, Australia, Commonwealth Department of Health, 1980.

0017. PRINCE HENRY HOSPITAL, Department of Medicine, Little Bay, New South Wales 2036, Australia. UNIVERSITY OF NEW SOUTH WALES, Kensington, New South Wales 2033, Australia.

Project Title:
Epidemiology of Occupational Respiratory Diseases.

Principal Investigators:
Gandevia, B.; Field, G.B.; Owen, P.

Objective:
To conduct an epidemiological investigation of occupational respiratory hazards; determine the relationship, if any, of smoking to clinical and functional data.

Methods or Approach:
Although individual and clinical cases are studied, the more valuable research approach is epidemiological and involves surveys of total occupational populations. In addition to conventional questionnaires, clinical examination, and radiology, an extensive range of lung function tests is conducted by using a mobile laboratory.

Results to Date:
Studies have been completed on working populations exposed to aluminum smelting fumes, proteolytic enzymes in the detergent industry, oil refinery processes, asbestos mining and milling, fiberglass production, and cotton dust. A 10-year followup study of lung mechanics and transfer factor in asbestos workers is currently nearing completion. Except with cotton, the results generally confirm an association between smoking, functional disturbance, and radiographic changes, although smokers tend to leave some occupations with a respiratory hazard.

Future Plans:
Data are continually being accumulated; the most recent source is workers dealing with animals and insects.

Project Dates:
1970–continuing.

Financial Support:
Prince Henry Hospital; Workers' Compensation Board, New South Wales.

0018. PUFFABILITY PEOPLE, INC. 16 Sulman Road, Wembley Downs, Western Australia 6019, Australia.

Project Title:
Community Lung Function. The Effects of Passive Smoking on Lung Function.

Principal Investigators:
Dunn, A.G.; Dunn, P.A.
Objective:
To (1) ascertain normal lung function parameters for the community; (2) search for independent variables affecting lung function; and (3) determine effects of passive smoking on lung function.
Methods or Approach:
Community-based computerized lung function analysis will be used as the basis of the cross-sectional survey. Lectures will also be given.
Results to Date:
Approximately 10,000 persons have been tested. Preliminary analysis on 3,000 subjects shows the expected rapid decline in many parameters in smokers. A similar but less marked reduction in lung function was found in nonsmokers in some parameters. Passive smokers (nonsmokers exposed to large quantities of cigarette smoke) had a 7 percent reduction in forced expiratory volume in 1 sec (males) and reductions of 9 and 7 percent in forced mid expiratory flow in males and females, respectively. All reductions were significant or highly significant.
Project Dates:
April 1983–December 1986.
Financial Support:
State Smoking and Health Project, Western Australia.

0019. PUFFABILITY PEOPLE, INC., 16 Salman Road, Wembley Downs, Western Australia 6019, Australia.

Project Title:
The Breathe Easy Project.

Principal Investigators:
Dunn, A.G.; Dunn, P.A.
Objective:
To reduce the number of children who start to smoke by encouraging them to be nonsmokers rather than discouraging them from being smokers.
Methods or Approach:
Positive imagery in association with nonsmoking was identified and sports personalities (Puffability People) were utilized in association with "Breathing Easy." Television commercials were produced establishing the positive association, utilizing modern Breathe Easy music.
Results to Date:
Preliminary analyses of children suggest that positive imagery is popular and memorable; the message is clear to children although it utilizes the soft sell technique. It is possible that this positive approach may be a more successful way of communicating with children and adolescents and thus a more effective community health measure than more conventional antismoking campaigns.
Project Dates:
October 1984–continuing.

0020. QUEEN ELIZABETH II MEDICAL CENTRE, Nedlands, Western Australia 6009, Australia.

Project Title:
Volume Changes in Tobacco Advertising in Western Australian Newspapers in Response to Proposed Government Legislation.

Principal Investigators:
Castleden, W.M.; Nourish, D.J.; Woodward, S.D.
Objective:
To examine cigarette advertising volume in three major daily West Australian newspapers for July through October, 1981 and 1983.
Methods or Approach:
There have been suggestions that the tobacco industry utilizes its financial resources to influence newspaper and magazine editors not to publish unfavorable stories. From July to October 1983, the industry was under threat because its freedom to advertise cigarettes in Western Australia was undergoing parliamentary and public scrutiny and debate. In addition to the three major daily newspapers in Western Australia, two Brisbane (Queensland) newspapers were examined. All cigarette, tobacco, and cigar advertisements were reviewed, and information on page number, size (full or partial page), brand, and whether advertisement was in black and white or color was recorded.
Results to Date:
The volume of cigarette advertising was much higher in Western Australia in 1983 than in 1981. In addition, volume increased markedly when legislative action was threatened, and remained at very high levels until the bill failed to pass. In the Queensland papers, the number of cigarette advertisments declined between 1981 and 1983.
Future Plans:
Since it has been established that the population of Queensland is subjected to considerably less advertising than than people in Western Australia, it is proposed that smoking rates in school children in the two states be investigated to establish the connection between cigarette advertising and childhood smoking habits.
Project Dates:
March 1984–December 1985.

0021. QUITS SMOKING CESSATION SERVICE, Health Promotion Center, Childers Street, Canberra City, Australian Capital Territory 2601, Australia.

Project Title:
Evaluation of Community Smoking Cessation Programmes.

Principal Investigator:
Whyte, H.M.
Objective:
To define characteristics of smokers who seek help from a smoking cessation service and succeed before becoming involved in any formal therapeutic program; compare effectiveness of five different smoking cessation programs over a 12-month followup period; and define characteristics of smokers who succeed in becoming and remaining nonsmokers over a 12-month period so that better subject selection can be made to maximize chances of success in cessation of smoking.
Methods or Approach:
Clients enrolled in the QUIT program are screened and 60 percent are selected for different program treatments. Participants are randomly allocated to one of five programs (at least 70 persons in each group). Self-completed reports of clients at the end of the program are analyzed and results compared.
Results to Date:
At the end of the program a dramatic reduction in smoking had occurred; however, recidivism was high during the next 3 months, emphasizing the need for support. The significant drop in smoking between first and second visit (18.6 percent) before attending a program highlights the value of established services involved in smoking cessation. The cohort group (those for which complete sets of data were available for first and second visit, end of program, and 3-, 7-, and 12-month followup) had more success than the total study population. The cohort group showed more geographic stability and had

more personal contact, which could have been crucial factors in success. Data from 12-month followup showed 64.9 percent of the total sample and 69.3 percent of the cohort recorded positive changes in smoking behavior.

Project Dates:
August 1979–June 1983.

Financial Support:
Commonwealth Department of Health, Australia (HSR 118).

0022. ROYAL CHILDREN'S HOSPITAL, Department of Paediatrics, Parkville, Victoria, 3052 Australia.

Project Title:
Natural History of Childhood Asthma in Adult Life.

Principal Investigators:
Phelan, P.D.; Olinsky, A.; Pain, M.C.F.

Objective:
To document prevalence of asthma and its natural history; determine factors associated with amelioration and deterioration.

Methods or Approach:
Subjects with a past history of wheezing were randomly selected at age 7 and have been followed up at 10, 14, and 21 years of age. In 1985, they will be reviewed at age 28. A detailed history and examinations have been conducted on factors associated with asthma and its therapy. Pulmonary function tests, including spirometric measures of vital capacity and forced expiratory volume in 1 sec and lung volumes have been recorded. At age 21, bronchial reactivity was assessed by exercise and histamine; at age 28, histamine alone will be used. At age 28, a particular aim will be to determine what percentage of subjects have developed irreversible airways obstruction and attempt to determine contributing factors, including cigarette smoking.

Results to Date:
Findings indicate that 20 percent of children have asthma. About 50 percent of those with trivial wheezing apparently cease wheezing by the age of 10; however, 60 percent of these continue to demonstrate bronchial reactivity in early adult life. Also, 75 percent of those with frequent episodic asthma and 95 percent of those with chronic asthma in childhood continue to have asthma in early adult life; over 80 percent in each group show bronchial reactivity. At age 21, 40 percent of control subjects and 40 percent of those with minor asthma were smoking more than five cigarettes/day. Of those with severe asthma, 48 percent were smoking more than five cigarettes/day.

Future Plans:
It is hoped that the project can be continued until subjects are in their forties or fifties.

Project Dates:
1964–continuing.

Financial Support:
NHMRCA.

0023. ROYAL CHILDRENS HOSPITAL, Department of Thoracic Medicine and Department of Paediatrics, Flemington Road, Melbourne, Victoria 3052, Australia.

Project Title:
Longterm Follow Up of RSV Bronchiolitis and Its Relationship to Asthma.

Principal Investigators:
Sly, P.D.; Landau, L.I.; Olinsky, A., et al.

Objective:
To determine relationship between respiratory syncitial virus (RSV) bronchiolitis and subsequent asthma; identify factors that may allow detection of underlying asthmatic tendency.

Methods or Approach:
Infants under 6 months of age diagnosed with RSV bronchiolitis have been enrolled, and lung function studies have been performed in 50 infants. Subjects will be followed yearly by questionnaire; lung function studies will be repeated at 8 years of age. Bronchodilator responsiveness was assessed by measuring specific respiratory conductance before and after bronchodilation.

Results to Date:
Data from 2-year followup show more than 80 percent of the infants have had further wheezing and symptoms suggestive of asthma. Among families of infants with bronchiolitis, 83 percent had members who smoked, a proportion higher than would be expected in the study community (54 percent of the mothers were smokers). Babies of mothers who smoke had lower specific conductance than those of nonsmoking mothers, but there was no difference in bronchodilator response.

Project Dates:
June 1982–1991.

Financial Support:
Royal Children's Hospital, Melbourne; Asthma Foundation of Victoria, Australia.

0024. SOUTH AUSTRALIAN HEALTH COMMISSION, HEALTH PROMOTION SERVICES, State Bank Building, 158 Rundle Mall, Adelaide, South Australia 5000, Australia.

Project Title:
Evaluation of the South Australian Pilot Stop Smoking Programme in Whyalla, Port Augusta, and Port Pirie, March 1983.

Principal Investigators:
Wilson, D.; Wakefield, M.

Objective:
To evaluate a pilot intervention stop smoking program using media and community services.

Methods or Approach:
A household survey was conducted in study areas (Whyalla, Port Pirie, Port Augusta) and in the control town (Mount Gambier) prior to and following the intervention program (cohort study). Sample size was 1,042 persons in the study area and 457 in the control town.

Results to Date:
Results show that there was a statistically significant difference in the number of people who stopped smoking in the test area compared with the control area 3 months after the start of the campaign.

Project Dates:
March 1983–continuing.

Financial Support:
South Australian Health Commission.

0025. SOUTH AUSTRALIAN INSTITUTE OF TECHNOLOGY, ELTON MAYO SCHOOL OF MANAGEMENT STUDIES, North Terrance, Adelaide, South Australia 5001, Australia.

Project Title:
Smoking Behaviour of Nurses in Hospital and Tertiary College Training Programs.

Principal Investigators:
Harris, M.; Woodward, A.
Objective:
To test the hypothesis that nurses trained in a conventional, hierarchial hospital program are more likely to take up smoking than nurses trained as tertiary students in a college program.
Methods or Approach:
Graduating students from two major teaching hospitals and one tertiary college in South Australia with a training program for nurses completed written questionnaires about smoking habits.
Results to Date:
Results are not yet available.
Project Dates:
October 1984–February 1985.
Financial Support:
South Australian Institute of Technology, Elton Mayo School of Management Studies.

0026. ST. VINCENT'S HOSPITAL, SMOKER'S CLINIC, Darlinghurst, Sydney, New South Wales 2010, Australia.

Project Title:
Investigation of the Nicotine Withdrawal Syndrome.

Principal Investigator:
Bittoun, R.
Objective:
To detail the physiological and psychosocial symptoms of nicotine withdrawal to help prevent relapse; study changes that occur in sleep, respiratory function, incidence of mouth ulcers, and general malaise that are commonly reported with smoking cessation.
Methods or Approach:
Data on 600 smokers entering a smoking cessation treatment program are collected by questionnaires before treatment and at 3 and 6 months posttreatment. Nonsmoking status is corroborated by biochemical assays, usually urine cotinine.
Results to Date:
Findings to date indicate increased incidence of cough and colds within the first few months after quitting. It is hypothesized that this is due to local effects of nicotine on ciliary activity and its suppression of the cough reflex. Changes in sleep occurred in the form of hyposomnolence or hypersomnolence, changes that stabilize by 3 months. There was increased incidence of mouth ulcers, which was not related to usage of nicotine gum or any other therapy or intervention.
Project Dates:
June 1983–1985.

0027. ST. VINCENT'S HOSPITAL, SMOKER'S CLINIC, Darlinghurst, Sydney, New South Wales 2010, Australia.

Project Title:
Multi-Faceted Nicotine Chewing Gum Trial.

Principal Investigators:
Bittoun, R.; Clarke, J.C.; Bryant, D., et al.
Objective:
To enhance the long-term success rate of nicotine chewing gum (Nicorette) by including other methods of smoking cessation such as rapid smoking (a conditioned aversion technique).
Methods or Approach:
A double-blind trial using 2 mg or 4 mg nicotine gum was undertaken with 200 smokers to establish efficacy of gum for smoking cessation. Subjects were randomly assigned to treatment programs. Rapid smoking (or rapid puffing) was used as an adjunct to the gum. Carboxyhemoglobin assays were used to verify self-reports.
Results to Date:
Results to date show that effects of nicotine gum remain constant with or without rapid smoking as added treatment.
Project Dates:
June 1984–December 1985.
Financial Support:
Glaxo Australia; A.B. Leo Foundation, Sweden.

0028. SYDNEY HOSPITAL, KANEMATSU MEMORIAL INSTITUTE, Sydney, New South Wales 2000, Australia.

Project Title:
Immunogenicity of Tobacco Smoke Production in Human Subjects.

Principal Investigator:
Hersey, P.
Objective:
To (1) determine whether the association between vascular disease and smoking may be due to production of antibodies to smoke products in serum of smokers (present mainly in the form of immune complexes); (2) define the nature of chemicals in tobacco smoke recognized by immunoglobulin G (IgG) antibodies in human sera from smokers and nonsmokers; (3) compare the antigens with those in extracts of other solanaceous plants in the diet; and (4) assess skin test reactivity of smokers and nonsmokers to extracts of cigarette smoke and compare this with serological reactivity to the extracts.
Methods or Approach:
Preliminary studies concentrated on antigens present in smoke considered most relevant to disease states in humans. Water soluble extracts of smoke were used to examine incidence of antibodies in smokers, nonsmokers, and children, using nephelometric assays. Extracts were also used to develop an enzyme-linked antibody assay. Characterization of the antigens concerned was conducted by gel filtration and comparisons were made with ammonium sulphate precipitated extracts of tomato leaves. Screening assays for carbohydrate suggested that the antigens were not carbohydrate in nature. The antibody class in serum against smoke products were defined as IgG, but tests for IgE antibody were not in included in the analysis.
Results to Date:
Data show that 30 percent of smokers and 14 percent of nonsmokers had antibodies to soluble extracts of tobacco smoke detectable in sera. It was also found that antibody activity against smoke extracts cross-reacted with extracts of other solanaceous plants such as tomato leaves. Densitization against antigens from dietary sources may explain detection of antibodies in nonsmokers and children, as no correlation could be found with degree of exposure to passively inhaled cigarette smoke; however, such exposure could not be excluded. Higher incidence of detectable antibodies in smokers and the decline in antibody titre after cessation of smoking were strong evidence that smoking was responsible, at least in part, for appearance and maintenance of antibody to smoke extracts. Evidence also suggests that antibody activity was related to incidence of immune complexes in the circulation of smokers and that much of antibody activity in serum is present in the form of immune complexes, suggested by the demonstration that antibody was shown to be of the IgG class by affinity chromatography, but separated in large molecular weight fractions by gel filtration.

Project Dates:
January 1981–December 1983.
Financial Support:
ATRF.

0029. UNIVERSITY OF ADELAIDE, Department of Community Medicine, North Terrace, Adelaide, South Australia 5001, Australia.

Project Title:
A Randomized Controlled Trial of a Health Education Program to Reduce Passive Smoking in Infancy.

Principal Investigator:
Woodward, A.
Objective:
To determine whether a simple health education program would alter smoking habits of parents of newborns and reduce tobacco smoke exposure of infants.
Methods or Approach:
The trial included block randomization of participants into a treatment group or into one of two control groups. Mothers in the treatment group received literature and one counseling session during their hospital stay, and an additional telephone contact 1 month later. All participants were contacted after 3 months and questionnaire data were collected. Urine samples were taken from mothers and infants for measurement of cotinine levels.
Results to Date:
Preliminary data do not show a significant difference between treatment and control groups in parental smoking patterns.
Project Dates:
July 1984–July 1985.
Financial Support:
South Australian Health Commission.

0030. UNIVERSITY OF ADELAIDE, Department of Community Medicine, Adelaide, South Australia 5001, Australia.

Project Title:
Controlled Trial of a Health Education Program to Reduce Passive Smoking in Infancy.

Principal Investigator:
Woodward, A.; Grgurinovich, N.; Owen, N.
Objective:
To determine if a simple health education intervention, with personal followup and support, provided to parents shortly after the birth of their child, would reduce exposure of infants to tobacco smoke.
Methods or Approach:
The 180 participants were allocated, by month of birth, to one of two control groups (no interview and interview) or to the treatment group (interview and health education program). The treatment group also received followup phone calls and letters. Subjects in all groups will be interviewed 3 months after infant's birth. Outcome is assessed by self-reported smoking behavior and biochemical measures (cotinine:creatinine ratios in maternal and infant urine). Breast milk specimens are also analyzed for nicotine.
Results to Date:
Project is in a preliminary phase.
Project Dates:
June 1984–January 1985.
Financial Support:
South Australian Health Commission.

Reference:
Woodward, A.; Miles, H.; Grgurinovich, N. "Cotinine in the Urine of Smokers' Infants." *Lancet* 2(8408):935, October 1984.

0031. UNIVERSITY OF MELBOURNE, Department of Clinical Psychology, Austin Hospital, Heidelberg, Victoria 3084, Australia. WESTMEAD HOSPITAL, Department of Psychiatry, Westmead, New South Wales 2145, Australia.

Project Title:
Cerebral Effects of Tobacco Smoking.

Principal Investigators:
Milgrom-Friedman, J.; Meares, R.A.
Objective:
To (1) investigate the possibility that tobacco smoking alters sensory input regulation; (2) compare the effects of tobacco smoking and chewing nicotine gum on measures of sensory input regulation; and (3) determine the influence of personality factors on these variables and the differences between smokers and nonsmokers.
Methods or Approach:
Male smokers and nonsmokers have volunteered for the following procedures: (1) cortical-evoked potential recordings to light and sound; (2) measures of habituation rates of galvanic skin responses to sound stimuli; (3) ischemic pain onset and tolerance in response to a pneumatic blood pressure cuff; (4) paper and pencil questionnaires (Eysenck Personality Inventory and McGill Pain Questionnaire); and (5) allocation to conditions of smoking, smoking deprivation, and chewing 2 mg nicotine or placebo gum.
Results to Date:
Tobacco smoking seems to increase the individual's capacity to screen out meaningless auditory stimuli. Tobacco smoking also seems to affect stimulus intensity modulation of sound in a similar way. However, the visual system seems to be affected in an opposite way. Visually evoked potentials are enhanced by tobacco smoking whereas auditory evoked potentials are reduced. These effects seem to be mediated by nicotine and have been reproduced in subjects chewing nicotine gum. An interesting finding has been that smokers chewing placebo gum believing it to be nicotine have evoked potential changes similar to those produced by smoking. This is not the case for nonsmokers. Deprivation of cigarettes has also been found to diminish smokers' sensitivity to pain significantly below that of nonsmokers, and smoking cigarettes tends to heighten sensitivity up to, or beyond, the level of nonsmokers. Finally, the personality dimension of extraversion has been found to interact with the effect of nicotine on visual cortical processing in both smokers and nonsmokers.
Project Dates:
1973–1983.
Financial Support:
ATRF.
Reference:
Milgrom-Friedman, J.; Penman, R.; Meares, R. "A Preliminary Study on Pain Perception and Tobacco Smoking." *Clinical and Experimental Pharmacology and Physiology* 10(2):161-169, March-April 1983.

BEST COPY AVAILABLE

0032. UNIVERSITY OF MELBOURNE, REPATRIATION GENERAL HOSPITAL, Department of Surgery, Heidelberg, Victoria 3081, Australia.

Project Title:
The Role of Alcohol, Tobacco, and Nutrition as Determinants of Oral Cancer and Oesophageal Cancer.

Principal Investigators:
Kune, G.A.; Kune, S.; Watson, L.
Objective:
To determine role of alcohol consumption, tobacco intake, and dietary intake as determinants of squamous cell carcinomas of the oral cavity and esophagus.
Methods or Approach:
Two separate case-control studies will be conducted, using three controls for each case. It is expected that 50 oral cancer cases and 30 esophageal cancer cases will be recruited.
Results to Date:
Project is in a preliminary phase.
Project Dates:
1984–December 1985.
Financial Support:
University of Melbourne.

0033. UNIVERSITY OF MELBOURNE, REPATRIATION GENERAL HOSPITAL, Department of Surgery, Heidelberg, Victoria 3081, Australia.

Project Title:
The Melbourne Large Bowel Cancer Study.

Principal Investigators:
Kune, G.A.; Kune, S.; Watson, L.
Objective:
To (1) determine incidence of colorectal cancer in Melbourne; (2) determine distribution of cases by sex, site, subsite, religion, and country; (3) determine risk relationship with nutrition, alcohol consumption, and tobacco use, using bowel habits, parity, and psychosocial factors as determinants; and (4) establish survival rates of colorectal cancer.
Methods or Approach:
An incidence study that covered 1 year yielded 1,150 cases. A case-control study (715 cases, 725 community and 159 hospital controls) was also conducted. A survival study was made of the incident cases.
Results to Date:
Data are being analyzed; results are not yet available.
Project Dates:
1980–1986.
Financial Support:
University of Melbourne.

0034. UNIVERSITY OF MELBOURNE, REPATRIATION GENERAL HOSPITAL, University Department of Surgery, Heidelberg, Victoria 3081, Australia.

Project Title:
Risk Factors Other Than Tobacco as Determinants of Lung Cancer.

Principal Investigators:
Kune, G.A.; Kune, S.; Watson, L.
Objective:
To examine nutritional factors, alcohol consumption, family history of lung cancer, and occupational exposure as determinants of lung cancer.
Methods or Approach:
A case-control study of male lung cancer patients will be conducted, using one control for each of an expected 100 cases. Tobacco habits will also be recorded.
Results to Date:
Project is in a preliminary phase.
Project Dates:
1984–December 1985.
Financial Support:
University of Melbourne.

0035. UNIVERSITY OF MELBOURNE, 159 Barry Street, Melbourne, Victoria 3053, Australia.

Project Title:
Health Watch: The Australian Petroleum Industry Health Surveillance Programme.

Principal Investigators:
Christie, D.; Robinson, K.R.; Gordon, I.
Objective:
To determine the relationship between occupational exposure and subsequent cancer occurrence; examine smoking habits as confounding variable.
Methods or Approach:
A concurrent prospective study is being conducted among 12,000 employees in the Australian petroleum industry (total population in Australia). A resurvey in 1986 will provide data on temporal changes in smoking behavior. A cohort analysis is being carried out on prevalence data.
Results to Date:
Smoking behavior in this male industrial population differs from the general population survey samples only in that lower smoking rates are found in younger age groups.
Project Dates:
February 1981–continuing.
Financial Support:
Australian Institute of Petroleum Ltd.

0036. UNIVERSITY OF MELBOURNE, REPATRIATION GENERAL HOSPITAL, Department of Surgery, Heidelberg, Victoria 3081, Australia.

Project Title:
Determinants of Pancreas Cancer.

Principal Investigators:
Kune, G.A.; Kune, S.; Watson, L.
Objective:
To examine nutrition, alcohol consumption, tobacco use, and family history of pancreatic cancer as risk factors or determinants of pancreatic cancer.
Methods or Approach:
A case-control study will be conducted. A total of 50 cases is anticipated.
Results to Date:
Project is in a preliminary phase.
Project Dates:
1983–December 1985.
Financial Support:
University of Melbourne.

0037. UNIVERSITY OF NEW SOUTH WALES, SCHOOL OF COMMUNITY MEDICINE, P.O. Box 1, Kensington, Sydney, New South Wales 2033, Australia.

Project Title:
Evaluation of the Use of Nicotine Chewing Gum as an Adjunct

to General Practitioner Intensive Intervention or Brief Advice to Stop Smoking.

Principal Investigators:
Richmond, R.L.; Webster, I.W.
Objective:
To compare abstention rates of four groups of smoking patients in a group general practice; evaluate efficacy of a predictive scale to assess likely abstainers.
Methods or Approach:
The study will be conducted in a group general practice in Sydney. Patients who smoke will be randomly allocated to one of four groups. Group 1 will receive intensive intervention by the doctor, which will consist of relating objective measures (saliva cotinine and lung function tests) to health effects of smoking, a book, nicotine gum, and followup visits. Group 2 will receive intensive intervention, followup visits, and the book. Group 3 will receive only brief advice by the doctor to quit smoking and a prescription for nicotine gum. Group 4 will receive no intervention (controls).
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–December 1986.
Financial Support:
Glaxo Pharmaceutical Company.

0038. UNIVERSITY OF NEW SOUTH WALES, SCHOOL OF COMMUNITY MEDICINE, Kensington, Sydney, New South Wales 2033, Australia.

Project Title:
Evaluation of General Practitioners Use of a Smoking Cessation Program.

Principal Investigators:
Richmond, R.L.; Webster, I.W.
Objective:
To (1) develop and evaluate a program of smoking cessation based in general practice; (2) identify predictors of abstention; and (3) develop a predictive scale for general practitioners (GPs) to assess likely abstainers.
Methods or Approach:
In the project, conducted in a four-man general practice in Sydney, patients were randomly allocated, according by day of attendance, to treatment (100 smokers), control group 1 (100 smokers), or control group 2 (200 nonsmokers). The intervention program focused on attitude and behavior change, GP support and encouragement, and followup. Major components were six visits to the GP in 6 months; self-monitoring of smoking in a daily diary during the first week; patient education in the second week, relating blood carboxyhemoglobin (COHb) and cotinine and lung function test results to smoking-related diseases; program handbook for GPs; cessation manual for patients; and advice on withdrawal symptoms, weight management, and substitutes or alternatives to smoking.
Results to Date:
Abstinence rate at 6-month followup was 33 percent in the treatment group compared with 3 percent in controls. Self-reports of smoking status were validated by blood tests. Abstinence rate remained stable, indicating that the initial impact of the program was maintained. Blood levels of COHb, cotinine, and SCN per cigarette smoked were higher at 6 months in continuing smokers than at entry, despite a 30 percent decrease in stated cigarette consumption. Entry characteristics that were the most consistent predictors of abstention at 6 months were low to moderate dependence on cigarettes, high motivation to quit, dissatisfaction with health, and low blood concentrations of tobacco products. Based on these entry characteristics, a scale for predicting likely abstainers was developed.
Future Plans:
Workshops are being organized for teaching the cessation program to GPs. Program components have been revised and a stop smoking kit has been developed for GPs.
Project Dates:
January 1981–December 1984.
Financial Support:
University of New South Wales, School of Community Medicine; National Heart Foundation of Australia (G 1514).

0039. UNIVERSITY OF NEWCASTLE, New South Wales 2308, Australia.

Project Title:
Lung Cancer Mortality in Australia, Canada and United Kingdom, and Cumulative Tar Exposure.

Principal Investigators:
Gibberd, R.W.; Doyle, E.
Objective:
To predict the number of lung cancer deaths which will be avoided with different levels of tobacco consumption for 1985-2030.
Methods or Approach:
First, the tar exposure by sex and cohort for the Australian population from 1925 was estimated. Tabulations produced are similar to those of the Tobacco Research Council. Second, the actual, as opposed to reported, lung cancer mortalities were estimated, since improvements in standards of diagnosis have affected the recorded lung cancer death rates. An index which estimates these changes will be determined. Finally, the relationship between tar exposure and lung cancer mortality was determined and used to estimate reduction in lung cancer deaths if consumption was reduced.
Results to Date:
Data for the countries have been collected, and analysis of results shows that lung cancer mortality rates can be predicted using the variables of age and cumulative tobacco consumption. There appears to be no cohort effect and only slight differences between countries. Further analysis was used to predict future lung cancer mortality.
Project Dates:
1980–1983.

0040. UNIVERSITY OF NEWCASTLE, FACULTY OF MEDICINE, Newcastle, New South Wales 2308, Australia.

Project Title:
Hunter Region Childhood Smoking Prevention Study.

Principal Investigator:
Leeder, S.R.
Objective:
To (1) determine at what ages children begin smoking; (2) identify which children are most likely to acquire the habit; and (3) determine what forms of intervention are likely to be effective in prevention of smoking.
Methods or Approach:
Prevalence of smoking was assessed in 6,224 children (10 to 12 years of age) in the Hunter Region of New South Wales. Confidential, self-administered questionnaires were given to children, parents, and teachers to determine smoking habits and peer group and social environment and to identify social

and personal factors associated with childhood smoking. Logistic regression was used to determine the relative importance of key factors in relation to the proportion of smokers in the "recent" and "regular" smoking categories. A 1-year randomized trial was used to evaluate effectiveness of a smoking prevention program. Factors associated with changes in smoking behavior over the 12-month period were determined for children who became smokers (adopters), those who remained nonsmokers, those who quit smoking (quitters), and those who remained smokers.

Results to Date:
Smoking by friends was the best predictor of a child's smoking status, followed by (in order) approval of advertising, siblings' smoking behavior, amount of money available to spend weekly, sex, age, and parents' smoking habits. Other factors (size of family, position of child in the family, country of parents' birth, father's occupation, having a single parent, and urban or nonurban location of schools) were all significantly associated with smoking prevalence. Girls and nonsmokers had less favorable attitudes toward smoking and advertising than boys and smokers. Significant differences in knowledge were found between categories of smokers. Most children claiming not to smoke disapproved of advertising and did not intend to smoke in the future. Among current smokers, some with neutral or favoring attitudes were ambivalent about future smoking. Data suggest that intervention into the field of cigarette advertising may be the most direct and effective means of reducing the prevalence of smoking in children. There were no significant differences in smoking behavior following the 12-month prevention program between treatment and control groups. Effectiveness varied with sex and age, being most successful among older girls and least successful among younger boys. Attitude changes paralleled changes in smoking behavior. Changes in knowledge differed only slightly between treatment and control groups. Inadequate implementation by some teachers may have been associated with adverse effects on children's behavior, attitudes, and knowledge.

Financial Support:
NHMRCA; New South Wales State Cancer Council; University of Newcastle.

References:
(1) Hardes, G.R.; Alexander, H.M.; Dobson, A.J., et al. "Cigarette-Smoking and Drug Use in Schoolchildren in the Hunter Region, New South Wales. 1. Tobacco, Alcohol and Analgesic Use in 10- to 12-Year-Old Primary Schoolchildren (1979)." *Medical Journal of Australia* 1:579-581, 1981. (2) O'Connell, D.L.; Alexander, H.M.; Dobson, A.J., et al. "Cigarette Smoking and Drug Use in Schoolchildren: II–Factors Associated With Smoking." *International Journal of Epidemiology* 10(3):223-231, 1981. (3) Lloyd, D.M.; Alexander, H.M.; Callcott, R., et al. "Cigarette Smoking and Drug Use in Schoolchildren: III–Evaluation of a Smoking Prevention Education Programme." *International Journal of Epidemiology* 12(1):51-58, 1983. (4) Alexander, H.M.; Callcott, R.; Dobson, A.J., et al. "Cigarette Smoking and Drug Use in Schoolchildren: IV–Factors Associated With Changes in Smoking Behaviour." *International Journal of Epidemiology* 12(1):59-65, 1983.

0041. UNIVERSITY OF QUEENSLAND, Department of Obstetrics and Gynecology, Clinical Sciences Building, Royal Brisbane Hospital, Brisbane, Australia 4029.

Project Title:
Smoking and Breast Feeding.

Principal Investigators:
Mackay, E.V.; Counsilman, J.J.; Copeland, R.M.

Objective:
To assess the relationship of smoking to breast feeding (knowledge, attitudes, and practices).

Methods or Approach:
Attitudes toward breast feeding were assessed by questionnaire in a cohort of 1,790 pregnant women. Information was related to relevant physical characteristics, health measures, other attitudes, environmental conditions, and behavioral attributes. Participants were reassessed 6 and 12 months after delivery to determine the success of breast feeding in relation to the variables studied, with emphasis on smoking behavior.

Results to Date:
Results are not yet available.

Project Dates:
1982–1985.

Financial Support:
University of Queensland.

0042. UNIVERSITY OF SYDNEY, WESTMEAD HOSPITAL, Department of Medicine, Sydney, New South Wales 2006, Australia.

Project Title:
Individual Susceptibility to Bronchogenic Carcinoma Among Cigarette Smokers - Detection by In Vitro Metabolic Tests.

Principal Investigator:
Farrell, G.C.

Objective:
To determine individual susceptibility to bronchogenic carcinoma among cigarette smokers.

Methods or Approach:
For each patient, data for increasing benzo(*a*)pyrene (BaP) radiolabeled binding to lymphocyte macromolecules was used to construct a double reciprocal Lineweaver-Burke plot and calculate values from Km and V_{max}. Three groups of male patients were studied: (1) 13 normal controls (nonsmokers or ex-smokers of >2 years' duration, mean age 63.5 years); (2) 6 ex-smokers with primary carcinoma of the lung (all had stopped for at least 2 months, mean age 62.8 years); and (3) 10 current smokers who had no evidence of lung cancer (mean age 51.2 years).

Results to Date:
There was no difference in Km in any of the groups; however, there was a highly significant ($p<0.01$) difference between lung cancer patients and both control groups in terms of the V_{max} of radiolabeled binding to TCA precipitable material. Data suggest that patients with lung cancer differ from healthy subjects (regardless of smoking status) with respect to capacity to bind putative carcinogenic material. BaP is known to be metabolized by rat microsomes to a variety of epoxides, quinones, phenols, and diols (including various combinations). Some of the intermediates are innocuous and some are carcinogenic, particularly diol epoxides. It may be that enzymatic variations predispose some individuals to accumulation of carcinogens and thus increase the chance of carcinogenesis.

Financial Support:
ATRF.

0043. UNIVERSITY OF SYDNEY, Department of Medicine, Sydney, New South Wales 2006, Australia.

Project Title:
The Mechanisms of Chronic Airflow Limitation in Smokers.

Principal Investigators:
Woolcock, A.J.; Peat, J.K.
Objective:
To (1) investigate whether cigarette smoke causes irreversible abnormality in bronchial smooth muscle in some smokers; (2) determine whether abnormality is associated with increased responsiveness to histamine; examine whether abnormality is the same as that found in asthmatics; and (4) determine whether abnormalities can be identified at an early stage by measuring bronchial responsiveness to histamine.
Methods or Approach:
In 1981, information on respiratory symptoms, smoking habits, and spirometric function was collected on 922 adults as part of the Busselton Population Survey. In a retrospective study, past data obtained at 3-year intervals between 1966 and 1978 will be analyzed with 1981 and 1984 data. For the 1984 prospective study, data on smoking habits, respiratory symptoms, and drug use were collected and spirometry, response to bronchodilator, and response to histamine were recorded.
Results to Date:
Results are not yet available.
Project Dates:
January 1984–December 1985.
Financial Support:
ATRF.

0044. UNIVERSITY OF SYDNEY, Department of Medicine, Sydney, New South Wales 2006, Australia.

Project Title:
The Effects of Respiratory Illness and Smoking on Sydney Children.

Principal Investigators:
Woolcock, A.J.; Leeder, S.R.; Peat, J.K., et al.
Objective:
To (1) establish whether abnormalities in lung function that develop in childhood persist into adult life; (2) obtain data on origins of chronic nonspecific lung disease; (3) assess importance of apparently mild infections in childhood; (4) obtain data on development of normal and abnormal lung function between childhood and full adult development; and (5) determine effect of cigarette smoking on lung function.
Methods or Approach:
In 1971, a questionnaire was administered to 6,599 high school students and 4,898 primary schoolchildren to collect information on area of residence, birthplace, family size and socioeconomic status, nationality, and respiratory illness (asthma and bronchitis). Students were interviewed annually until 1976, and dropouts were interviewed annually at local health centers. Height and weight were measured and a confidential interview about smoking habits was conducted. Lung function was measured using maximal expiratory flow volume curves.
Results to Date:
Bronchitis, serious enough to require treatment, was common in Sydney infants <2 years of age and significantly more frequent in males (approximately 8.5 percent) than in females (approximately 7.0 percent). Bronchitis in early childhood was associated with increased risk of both bronchitis and asthma during later childhood, and until the age of 14 years, males continued to have more bronchitis than females. Prevalence of asthma in infancy and childhood is higher than in most other countries, and is also more common in males than in females. The majority of children who reported asthma developed it for the first time before the age of 8 years, although it can occur at any time during childhood. Children in Sydney began smoking at about 13 years of age. By the age of 16, girls were smoking more than boys, and approximately 35 percent of all children were regular smokers. In early adolescence, social class, nationality of the father, and leaving school early were the most important factors determining smoking habits. In later adolescence, being given a cigarette by a parent and peer group smoking habits were the most important factors. In adolescent smokers, respiratory symptoms were more common in girls than in boys. However, prevalence of cigarette smoking among children with different respiratory illness histories was the same. Small but persistent changes in lung function were found in both males and females who had had bronchitis and/or asthma before the age of 2 years. Deficits remained at least until early adult life. Subsequent bronchitis over the course of the study had an effect in addition to early respiratory illness in reducing forced vital capacity. The effect declined with age in boys and increased with age in girls. Subsequent asthma had the greatest effect on lung function and the deficit increased as children approached adulthood. Deficits in lung function attributed to smoking were found in some children by the age of 14 years and were present after only 1 year of smoking ≥ 10 cigarettes/week. Changes in lung function occurred in children who smoked but who previously had normal lung function. Smoking in children who had a history of respiratory illness, especially asthma, was associated with more marked abnormalities of lung function.
Project Dates:
January 1971–December 1983.
Financial Support:
ATRF.

0045. UNIVERSITY OF TASMANIA, QUEEN ALEXANDRA HOSPITAL, Department of Obstetrics and Gynaecology, Argyle Street, Hobart, Tasmania 7000, Australia.

Project Title:
An Assessment of Smoking in Pregnancy.

Principal Investigators:
Correy, J.; Newman, N.; Curran, J.
Objective:
To (1) determine incidence of smoking in pregnant patients; (2) determine effects of smoking on various parameters of obstetric and perinatal performance; and (3) relate effects to age, parity, marital status, and socieconomic status.
Methods or Approach:
Since 1974, an obstetric and perinatal audit has been conducted on all patients in Tasmania. Data on smoking habits have been requested since January 1981. Details of alcohol ingestion and drug use are also included, allowing four groups to be identified: nonsmokers/nondrinkers; smokers/drinkers; nonsmokers/drinkers; and smokers/nondrinkers. Smokers are grouped into consumption categories: ≤ 10 cigarettes/day, 10 to 20 cigarettes/day, 20 to 40 cigarettes/day, and ≥ 40 cigarettes/day. Information was available for 60 percent of patients in 1981 and for over 90 percent of patients in 1984. The four groups were assessed in relation to average birth weight of infants, incidence of birth weight $<2{,}500$ g, incidence of prematurity, congenital anomalies, perinatal death, antepartum hemorrhage, and hypertension in pregnancy.
Results to Date:
Incidence of smoking was higher among young, unmarried women of lower socioeconomic status; alcohol consumption was higher in other groups. Birth weight was lower among infants of smokers and was not influenced by mild alcohol ingestion. Perinatal death was higher in smokers. There were

no differences in antepartum hemorrhage or congenital anomalies between groups. Hypertension and postpartum hemorrhage were lower in smokers.

Future Plans:
The accuracy of urine cotinine for predicting smoking habits will be determined and the possible role of passive smoking in obstetric performance will be investigated.

0046. UNIVERSITY OF WESTERN AUSTRALIA, Department of Psychology, Nedlands, Western Australia 6009, Australia.

Project Title:
Prediction of Relapse Following Voluntary Cessation of Smoking.

Principal Investigator:
Yates, A.J.

Objective:
To determine whether self-efficacy scores predict relapse following voluntary cessation of smoking; determine whether subjects identified as at high risk for relapse can be trained to increase self-efficacy to reduce risk.

Methods or Approach:
In a retrospective study, self-efficacy scores of subjects who quit smoking voluntarily 1 year earlier were measured. Discriminant function analysis was used to classify subjects as abstainers or nonabstainers and to determine ability of self-efficacy and other measures to classify subjects correctly; 92 subjects were evaluated. Using weights derived from the retrospective study, a prospective investigation was conducted with 32 subjects to identify subjects at high risk at time of cessation and devise training techniques to reduce risk.

Results to Date:
Analysis of 11 variables in the retrospective study data showed that a 14-item self-efficacy total score was as successful in classifying subjects as abstainers or recidivists as analyses involving all variables or the best combination of variables. In the prospective study, the same variables were administered shortly after quitting and before eventual status was known. The self-efficacy total score predicted status of all 15 subjects who had relapsed at 4-month followup, while the 7 subjects it had predicted would not relapse were still abstinent. The predictive power was maintained at 8-month followup and, at both followup points, proved superior to other measures.

Project Dates:
January 1983–completed.

Financial Support:
University of Western Australia.

0047. UNIVERSITY OF WESTERN AUSTRALIA, ROYAL PERTH HOSPITAL, Perth, Western Australia 6000, Australia.

Project Title:
Smoking, Platelets, and Vascular Prostanoids.

Principal Investigators:
Vandongen, R.; Taylor, R.; Beilin, L., et al.

Objective:
To determine the relationship between smoking, platelets, and vascular prostanoids.

Methods or Approach:
Platelet thromboxane production will be examined following acute and chronic tobacco exposure. Effects of plasma from smokers on vascular prostanoid synthesis will be studied, and plasma and urinary levels of platelet-activating factor will be determined in smokers and nonsmokers.

Results to Date:
Project is in a preliminary phase.

Project Dates:
December 1984–continuing.

Financial Support:
University of Western Australia.

0048. WESLEY HOSPITAL, QUEENSLAND FERTILITY GROUP LABORATORY, Coronation Drive, Auchenflower 4006, Australia.

Project Title:
Effect of Cigarette Smoking on Semen Quality in an Infertile Group.

Principal Investigator:
Harrison, K.L.

Objective:
To determine the nature of the association of cigarette smoking with reduced semen quality in different age groups in patients presenting to an infertility clinic.

Methods or Approach:
Results of detailed semen analysis are correlated with recent smoking habits and age.

Results to Date:
Overall semen quality is reduced in smokers compared with nonsmokers. Sperm density, motility, and quality of motility are the main parameters affected. Effects seem to be accelerated with increasing patient age.

Future Plans:
Findings will be subdivided for different periods of sexual abstinence.

Project Dates:
January 1983–December 1985.

Financial Support:
Queensland Fertility Group Laboratory.

AUSTRIA

0049. ELISABETHINEN HOSPITAL LINZ, Department of Pneumology, Fadingerstrasse 1, A-4020 Linz, Austria.

Project Title:
Lung Function and Environmental Conditions for School-Children.

Principal Investigators:
Schindl, R.; Aigner, K.; Wurtz, J., et al.
Objective:
To determine the effect of pollution on the health of schoolchildren living in towns compared with those living in the country.
Methods or Approach:
Lung function tests were conducted on 3,480 children with mobile flow volume method. Statistical evaluation utilized HB 66/40 with BMD program (University of California).
Results to Date:
Average of flow volume tests (midexpiratory flow at 50 and 25 percent) was in the normal range; however, results for children living in towns was significantly lower than for those living in the country. Also, girls had better lung function than boys. Data showed that 15 percent of country and 25 percent of town children had MEF_{25} below the normal range of 70 percent. Frequency of cough and dyspnea correlated with previous reports. There were more passive smokers among town children, and their medium MEF results were lower than for country children. There are also statistically significant differences in schoolchildren living in areas exposed to environmental emissions. Results offer the possibility of helping high-risk children, and the simple flow volume method is in demand for testing by school physicians.
Future Plans:
Data analysis will continue, particularly on the problem of passive smoking.
Project Dates:
1981–1982.
Financial Support:
Central Government of Upper Austria, Department of Health; Chemie-Linz-AG.
Reference:
Schindl, R. "Lung Function and Environmental Conditions for School-Children." *Weiner Medizinische Wochenschrift* 132(Suppl. 71):9-25, 1982.

0050. UNIVERSITY OF VIENNA, INSTITUTE OF HYGIENE, Kinderspitalgasse 15, A-1095 Vienna, Austria.

Project Title:
International Epidemiological Study of the Relationship Between Lung Cancer and Smoking.

Principal Investigators:
Kunze, M.; Vutuc, C.; Kunze, M.J.
Objective:
To investigate the relationship of the tar content of cigarettes with the risk of lung cancer in males and females.
Methods or Approach:
A retrospective case–control design was utilized; information was obtained through interviews. Data were analyzed for the relationship of age, duration, frequency of smoking, type of tobacco smoked, occupation, and drinking habits to lung cancer incidence and mortality.
Results to Date:
Among lung cancer patients, 93 percent of males and 63 percent of females were cigarette smokers, significantly more than among controls (64 percent of males and 21 percent of females). The dose–response relationship between lung cancer and smoking was evident; males smoking medium-tar cigarettes had a 59 percent lower relative risk (RR) compared with smokers of high-tar (≥ 24 mg tar) cigarettes. Patients who smoked low-tar (< 15 mg tar) cigarettes had RR 70 percent lower than that of high-tar smokers. Similar relationships in RR were found for female lung cancer patients. Results have been published.
Financial Support:
NCI (ECI-SHP-75-120).
References:
(1) Vutuc, C.; Kunze, M. "Lung Cancer Risk in Women in Relation to Tar Yields of Cigarettes." *Preventive Medicine* 11:713-716, 1982. (2) Vutuc, C.; Kunze, M. "Tar Yields of Cigarettes and Male Lung Cancer Risk." *Journal of the National Cancer Institute* 71(3):435-437, September 1983.

BANGLADESH

0051. BANGLADESH CANCER EPIDEMIOLOGY RESEARCH PROGRAM, Khan Mansion, 21 Nawab Katra, Dacca 2, Bangladesh.

Project Title:
Epidemiology of Lung Cancer.

Principal Investigators:
Rahim, M.A.; Ataharuddin Ahmed, Q.; Afroza, M.S., et al.
Objective:
To study the relationship between lung cancer and smoking in Bangladeshi nationals, including the quality of smoking material, quantity of smoking, method of smoking, and inhalation characteristics.
Methods or Approach:
Patients will be interviewed to obtain information on the variety of tobacco smoked (bidi, hubble-bubble, country-made chukka, plain, or filter-tipped), the amount smoked, duration of each smoking episode, and degree of inhalation. Questions have been designed to collect these data from the radiotherapy units in Bangladesh. All records will be collected by the Bangladesh Cancer Epidemiology Research Program for analysis.
Results to Date:
Recent publications have shown lung cancer ranks first in males and its average relative frequency is 16.54 percent. Under current protocol, through December 1981, approximately 1,600 lung cancer patients and matched controls have been interviewed.
Project Dates:
March 1976–1988.
Financial Support:
Bangladesh Association for Cancer Services.

0052. CANCER EPIDEMIOLOGY RESEARCH PROGRAM, Khan Mansion, 21 Nawab Katra, Dacca 2, Bangladesh.

Project Title:
Smoking Habit Among University Women.

Principal Investigator:
Rahim, M.A.
Objective:
To (1) review the situation in Bangladeshi female smokers studying in universities; (2) determine whether smoking habit will increase, decrease, or remain stationary during 10 years (1980-1990); (3) determine smoking material used; (4) determine the age at which smoking was started; and (5) determine from whom the subjects got the temptation to smoke.
Methods or Approach:
Questionnaires will be given to the students. After completing the forms, the students will return them by mail. Surveys will be conducted between January and July of each year.
Results to Date:
To date, 265 replies have been received and the data are being analyzed.
Project Dates:
January 1980–1990.
Financial Support:
Bangladesh Association for Cancer Services.

BARBADOS

0053. UNIVERSITY OF THE WEST INDIES, QUEEN ELIZABETH HOSPITAL, Faculty of Medicine, Bridgetown, Barbados.

Project Title:
Relation of Smoking, Alcohol and Marihuana Use to Hospital Morbidity and Mortality in Barbados.

Principal Investigators:
Fraser, H.S.; Mahoraj, D.
Objective:
To determine the relationship between smoking, alcohol consumption, and marijuana use and morbidity and mortality in a general hospital in a developing country (Barbados).
Methods or Approach:
A brief questionnaire will be administered to ascertain history of drug use in all patients admitted to adult medical and surgical wards and those seen in the casualty department. Correlations will be examined between drug use and age, sex, and diagnosis. Age-matched controls (nonsmokers, nondrinkers, etc.) will be compared with drug users.
Results to Date:
Preliminary results indicate a high incidence of alcohol-related disease and an apparent rapid increase in smoking-related disease, especially coronary disease.
Project Dates:
January 1985–April 1985.

0054. ACADEMIC HOSPITAL, Department of Endocrinology, De Pintelaan 185, 9000 Ghent, Belgium.

Project Title:
Influence of Smoking on Sex Hormone Levels in Young and Elderly Men.

Principal Investigators:
Vermeulen, A.; Deslypere, J.P.

Objective:
To determine chronic effects of smoking on plasma levels of sex hormones and gonadotropins in young, middle-aged, and elderly men.

Methods or Approach:
The cohort consisted of 70 men aged 20 to 39 years, 54 aged 40 to 59 years, and 57 aged 60 years or over. Sex hormones tested included testosterone, free testosterone, and estradiol; gonadotropins were LH and FSH. Blood was drawn for analysis. Smokers were those who smoked >5 cigarettes/day for >2 years; ex-smokers had stopped smoking for ≥ 2 years; nonsmokers had never smoked. Social background, weight, exercise level, and diet were similar in the three groups. Subjects taking any medication were excluded.

Results to Date:
In all three age groups smokers had significantly higher testosterone and free testosterone levels than nonsmokers; levels in ex-smokers were lower than in smokers. Estradiol levels were not significantly higher in smokers. No differences could be observed in gonadotropin levels.

Project Dates:
November 1982–May 1983.

Financial Support:
Fonds voor Wetenschappelijk Geneeskundig Onderzoek, Belgium (3.0009.82).

0055. ECOLE NORMALE SUPERIEURE, UN. DAKAR, Strudhoflaan 76, 2600 Berchem, Belgium.

Project Title:
Attitudes of Senegalese Adolescents Towards Tobacco Smoking.

Principal Investigators:
D'Hondt, W.; Vandewiele, M.

Objective:
To determine (1) frequency of smoking among adolescents; (2) age of smoking onset; (3) motivations and circumstances leading to smoking; (4) reactions to smokers' environment; and (5) perception of the consequences of tobacco smoking in Senegal.

Methods or Approach:
Interviews were conducted with 731 subjects (17 to 21 years of age) in two ways: a series of 413 interviews were carried out in various lycees throughout the regions during class hours and questionnaires were completed individually; (2) trained interviewers questioned volunteers among schoolchildren and noted the information according to the same prototype questionnaire.

Results to Date:
Results indicate that tobacco smoking is a widespread phenomenon among Sengalese adolescents for several reasons: (1) economic (intense advertising campaigns favoring smoking); (2) cultural (ambivalence of traditional attitudes of Western urbanization and the attractiveness of the Western way of life); and (3) psychological (traumas of modernization in a basically poor developing country). However, signs point to an effective prevention strategy aimed mainly at adolescent students and based on joint legal, scientific, cultural, and even religious action.

Future Plans:
Suggestions will be made on defining a global antismoking strategy for Africa.

Project Dates:
1980–1985.

Financial Support:
Belgian Cooperation Service.

Reference:
D'Hondt, W.; Vandewiele, M. "Attitudes of Senegalese Schoolgoing Adolescents Towards Tobacco Smoking." *Journal of Youth and Adolescence* 12(4):333-353, 1983.

0056. KATHOLICKE UNIVERSITEIT VAN LEUVEN, Department of Pathophysiology, B-3000 Leuven, Belgium.

Project Title:
Urinary Cadmium and Lead Excretion and Their Relation to Smoking and Blood Pressure in a Population With Low Exposure.

Principal Investigators:
Staessen, J.; Roels, H.; Bulpitt, C.J., et al.

Objective:
To determine urinary excretion of cadmium (Cd) and lead (Pb) in a random sample of households in a small Belgian town; investigate whether significant and independent associations can be found with smoking and blood pressure.

Methods or Approach:
A 4 percent random sample of all households in the town was identified. Blood pressure and anthropometric characteristics were measured on two separate occasions. A self-administered questionnaire was used to quantify tobacco consumption. Both 24-hour and spot urine tests were obtained for analysis.

Results to Date:
Urinary Cd (U-Cd) averaged 2.4 nmol/24 hours in 46 youths. U-Cd increased with age and was significantly higher in 57 adult men than in 59 women (9.3 nmol vs. 7.2 nmol/24 hours, $p<0.01$). Urinary Pb (U-Pb) averaged 28 nmol/24 hours in youths and increased with age. Adult men excreted more Pb than women (64.0 nmol vs. 40.0 nmol/24 hours, $p<0.001$). Among men, manual workers excreted more Cd than office workers (12.6 nmol vs. 7.5 nmol/24 hours, $p<0.05$), but excreted a similar amount of Pb (62.0 nmol vs. 61.0 nmol/24 hours). After adjusting for sex and age, U-Cd and U-Pb were not related to body weight or cigarette consumption. In simple regression analysis, U-Cd was positively correlated with both systolic ($r=+0.30$, $p<0.05$) and diastolic ($+0.38$, <0.01) blood pressure in women. However, after adjusting for other contributing variables, a weak but negative relationship became apparent between systolic pressure and U-Cd in women ($t=-2.21$, $p=0.033$) and between diastolic pressure and U-Cd in men ($t=-2.04$, $p=0.047$). U-Pb did not contribute to blood pressure variability in any of the sex-age groups.

Future Plans:
Results will be compared with other areas in Belgium where environmental exposure to cadmium is greater.

Project Dates:
September 1980–continuing.

Financial Support:
Nationaal Fonds voor Wetenschappelijk Onderzoek; Fond National de la Recherche Scientific Medical.
Reference:
Staessen, J.; Bulpitt, C.J.; Roels, H., et al. "Urinary Cadmium and Lead Concentrations and Their Relation to Blood Pressure in a Population With Low Exposure." *British Journal of Industrial Medicine* 41:241-248, 1984.

0057. UNIVERSITY OF GHENT, Department of Hygiene and Social Medicine, De Pintelaan 185, B-9000 Ghent, Belgium.

Project Title:
The Belgium Heart Disease Prevention Project (BHDPP).

Principal Investigators:
De Backer, G.; Kornitzer, M.
Objective:
To determine the effect of the Belgian Heart Disease Prevention Project (a randomized and controlled trial) on coronary heart disease incidence in middle-aged males.
Methods or Approach:
Information on smoking habits was collected from 1,035 participants in the intervention trial and from 1,087 controls.
Results to Date:
The validity of self-reported smoking behavior of subjects taking part in the intervention trial was confirmed. For ex-smokers and subgroups of smokers, no significant differences in thiocyanate concentrations were observed between intervention and control groups. In addition, in a subsample of smokers, differences in mean number of cigarettes smoked between intervention and control groups were parallel with significant differences in thiocyanate concentrations. A cutoff point of 0.45 mg/dL (77.6/µmol/L) gave a sensitivity of 82.1 percent among cigarette smokers in the control group and a specificity of 91.0 percent among nonsmokers. When intervention and control groups are compared in terms of self-reported smoking behavior, nonsignificant differences in mean thiocyanate concentration are observed for those who never smoked, ex-smokers, and actual cigarette smokers and in four different cigarette smoking categories.
Reference:
Kornitzer, M.; Vanhemeldonck, A.; Bourdoux, T., et al. "Belgian Heart Disease Prevention Project: Comparison of Self-Reported Smoking Behaviour With Serum Thiocyanate Concentrations." *Journal of Epidemiology and Community Health* 37(2):132-136, 1983.

0058. UNIVERSITY OF GHENT, Department of Hygiene and Social Medicine, De Pintelaan 185, B-9000 Ghent, Belgium.

Project Title:
Physical Activity, Physical Fitness and Coronary Heart Disease.

Principal Investigators:
De Backer, G.; Kornitzer, M.
Objective:
To study the relationship between physical activity at work and during leisure time, physical fitness, and incidence of coronary heart disease.
Methods or Approach:
The relationship between smoking and various coronary risk factors has been studied and the independent risk of coronary heart disease related to smoking has been identified using multivariate statistical analysis. This will be a prospective epidemiological study of the relationship of physical activity, physical fitness, and coronary heart disease. A comparable study has been carried out in Bratislava, Czechoslovakia, after standardization of methodology, and results from both countries will be compared.
Results to Date:
Results are not yet available.
Future Plans:
1975–1986.
Project Dates:
Belgium Ministry of Public Health.

0059. UNIVERSITY OF GHENT, Department of Hygiene and Social Medicine, De Pintelaan 185, B-9000 Ghent, Belgium.

Project Title:
Multinational Monitoring of Trends and Determinants of Cardiovascular Diseases (MONICA).

Principal Investigators:
De Backer, G.; Kornitzer, M.
Objective:
To monitor trends and determinants of cardiovascular diseases in Ghent and Charleroi, Belgium.
Methods or Approach:
MONICA Belgium is part of the international MONICA project, coordinated by the World Health Organization. In the communities of Ghent and Charleroi, incidence of acute myocardial infarction (AMI) is monitored using an AMI register. During the next decade, surveys will be conducted on changes in cardiac risk factors, including smoking habits.
Results to Date:
Project is in a preliminary phase.
Project Dates:
1983–1993.
Financial Support:
Belgium National Fund for Scientific Research; Belgium Ministry of Public Health.

BRAZIL

0060. ESCOLA PAULISTA DE MEDICINA, LABORATORIO FLEURY, Rua Botucatu, 740 Via Clementino, Sao Paulo CEP 04024, Brazil.

Project Title:
Effects of Smoking on Lung Alveolar Epithelial Permeability (AEP). Experimental Study With 99Tc-DTPA.

Principal Investigators:
Nery, L.E.; Sandoval, P.R.M.; Jardim, J.R.B., et al.
Objective:
To determine if smoking increases lung alveolar epithelial permeability in subjects with no alterations in clinical, x-ray, or pulmonary function tests.
Methods or Approach:
Subjects were 10 nonsmokers (median age 29.6 years) and 10 smokers (median age 27.1 years). The radioaerosol of 99^{Tc}DTPA (median aerodynamic diameter 1.1 μm±2.69 geometric SD) was provided to subjects who were seated with their backs against a gamma camera. During 2 min of loading, and for an additional 10 min, regional activity in three regions in each lung was calculated. The percent decline in activity (clearance rate-k percent/min) was evaluated over 7 min after deloading phase.
Results to Date:
Mean ± SE clearance (both lungs) in smokers (k: 2.93±1.06 percent/min) was significantly higher ($p<0.05$) than in nonsmokers (k: 1.17±0.30 percent/minute). The difference was even more striking when k was compared for the superior region of the lung in smokers and nonsmokers. Individual data show 9 of 10 values of k in smokers were higher than the highest value of nonsmokers. It is concluded that smoking leads to significant increase in lung alveolar epithelial permeability.
Future Plans:
Ceramic workers will be studied to determine whether silica exposure has any effect on alveolar epithelial permeability and an attempt will be made to identify workers at high risk for developing lung fibrosis.
Project Dates:
March 1984–November 1984.
Financial Support:
Laboratorio Fleury, Brazil.

CANADA

0061. ADDICTION RESEARCH FOUNDATION, 33 Russell Street, Toronto, Ontario M5S 2S1, Canada.

Project Title:
The Diffusion of Smoking Behavior: An Exploratory Analysis.

Principal Investigator:
Ferrence, R.G.
Objective:
To attempt to account for differences in cigarette smoking behavior using a diffusion model that has been used to describe adoption and discontinuance of various innovations.
Methods or Approach:
Evidence indicates that rates of use, heavy use, and cessation of smoking have varied over time, but that variation has not occurred uniformly among subcategories of the population. Rates have varied by age, sex, social class, occupation, and geographic region to different degrees at different times, and attempts to explain differences have not been wholly satisfactory because they do not account for changes over time among different groups. Secondary analyses, using Canadian data bases of smoking behavior, are being carried out. Various surveys conducted as part of the Canadian Labour Force survey and the Canada Health Survey (1978) are being used. Reconstructed cohort analysis will provide historical estimates of rates among sex-specific birth cohorts. The etiological significance of economic power, gender role, and health beliefs in predicting variations in smoking behavior will be examined.
Results to Date:
Results are not yet available.
Project Dates:
January 1984–December 1985.
Financial Support:
Addiction Research Foundation, Canada.

0062. AGRICULTURE CANADA, Box 186, Research Station, Delhi, Ontario N4B 2W9, Canada. ONTARIO MINISTRY OF AGRICULTURE AND FOOD, PESTICIDE RESIDUE TESTING LABORATORY, Guelph, Ontario N1G 2W1, Canada.

Project Title:
Pesticide Residues and Metals in Tobacco From Thirty-Four Ontario Farms.

Principal Investigators:
Elliot, J.M.; Frank, R.
Objective:
To determine levels of metals, organochlorine compounds, and organophosphorus compounds in the tobacco plant and soil.
Methods or Approach:
Samples of flue-cured tobacco from five stalk positions are obtained annually from an established survey of 34 farms. Standard laboratory procedures utilizing gas chromatography and atomic absorption spectroscopy are used to determine metals and components of the pesticides.
Results to Date:
Total DDT, chlordane, heptachlor epoxide, dieldrin, and total endosulfan in residues of flue-cured tobacco leaves of the middle stalk position were 0.49, 0.003, 0.007, 0.056, and 0.019 ppm, respectively. Residues of pesticides generally decreased with ascending stalk position. The decrease in level of DDT was from 0.58 to 0.49 ppm and the decrease in levels of endosulfan was from 2.6 to 0.019 ppm in the past 2 years, while levels of chlordane, heptachlor epoxide, and dieldrin have remained at levels previously determined. Levels of total DDT, chlordane, heptachlor epoxide, dieldrin, and total endosulfan in soils from fields on which tobacco leaves were grown were 1.84, 0.016, 0.009, 0.101, and 0.024 ppm, respectively. Levels of cadmium, copper, chromium, lead, manganese, nickel, and zinc in cured leaves of the middle stalk position were 1.7, 4.6,

1.3, 1.2, 125, 0.8, and 36 ppm, respectively. Levels of DTPA-extractable cadmium, copper, chromium, lead, manganese, nickel, and zinc in soils were 0.034, 0.66, 0.063, 0.012, 9.7, 0.104, and 1.78 ppm, respectively. There was no apparent correlation between DTPA-extractable metals in the soil and levels of metals in leaves of the middle stalk position.

Future Plans:
Further attempts will be made to correlate available metals with levels accumulated in cured leaves.

Project Dates:
1976–continuing.

Financial Support:
Agriculture Canada; Ontario Ministry of Agriculture and Food.

0063. ALBERTA INTER-AGENCY COUNCIL ON SMOKING AND HEALTH (CALGARY CHAPTER), TOM BAKER CANCER CENTRE, Department of Epidemiology and Preventive Oncology, 1331 29th Street, NW., Calgary, Alberta T2N 4N2, Canada.

Project Title:
Evaluation of a Kit Designed to Increase Smoke-Free Areas in the Workplace.

Principal Investigators:
Seaborn, J.; Fryers, P.; Leinweber, C., et al.

Objective:
To determine effectiveness of an information kit in increasing the proportion of designated smoke-free areas within the jurisdiction of employers who request the kit.

Methods or Approach:
A Smoking in the Workplace Kit (the Kit) has been developed for use by employers interested in the issue of designated smoke-free areas (SFA) in the workplace. The Kit contains information on health hazards associated with smoking, effects of passive smoking, economic costs of smoking, importance of the exemplar role of employers, and suggestions on increasing smoke-free areas. It also contains letters, that indicate that smoking is not a human rights issue and samples of existing corporate nonsmoking policies. The Kit will be promoted and distributed in January 1985 to all interested employers. A standard self-administered, questionnaire mailed after 12 months will evaluate effectiveness. The major variable (increase in SFA) will be measured by type of areas designated smoke-free, ratio of smoking to nonsmoking areas, and increase of SFA after exposure to the Kit. Additional variables will include form of SFA policy (written or verbal), including areas covered and enforcements, changes in hiring policies, employee feedback, and feedback from management. Information will also be collected on size of company, type of industry, number of employees, and ratios of white- to blue-collar workers, men to women, and nonsmokers to smokers. Physical characteristics (proportion of employees with private offices, number of workers in shared workplaces, and number of lunchrooms and coffee rooms) will also be recorded.

Results to Date:
The Kit has been distributed and evaluated on a pilot basis. Revisions have been made.

Project Dates:
January 1985–March 1986.

Financial Support:
Alberta Inter-Agency Council on Smoking and Health (Calgary Chapter).

0064. BRITISH COLUMBIA CANCER RESEARCH CENTRE, ENVIRONMENTAL CARCINOGENESIS UNIT, 601 West 10th Avenue, Vancouver, British Columbia V5Z 1L3, Canada.

Project Title:
Quantitating the Additive or Synergistic Action Between Cigarette Smoke and Industrial Contaminants.

Principal Investigators:
Rosin, M.P.; Stich, H.F.

Objective:
To quantitate additive, synergistic, or antagonistic effects of cigarette smoke and several agents to which human populations are exposed.

Methods or Approach:
A cigarette inhalation machine is used to produce smoke in a fashion that simulates human exposure patterns. Cell cultures are placed in a treatment chamber of the machine and smoke from one cigarette puff/min is blown into the chamber. The genotoxic effect is determined with two short-term assays: induction of chromosome aberrations in cultured Chinese hamster ovary (CHO) cells, and induction of gene conversion in *Saccharomyces cerevisiae* strain D7. To study multiple factor interactions, test cells can be exposed to various agents either prior to, during, or after exposure to cigarette smoke.

Results to Date:
Preliminary studies indicate that pretreatment of CHO cells with either chromate (potassium chromate K2CrO$_4$ and chromic chloride CrCl$_3$.6H$_2$O) or arsenic (sodium arsenite NaAsO$_2$ and sodium arsenate Na$_2$HAsO$_4$.7H$_2$O) followed by one to two puffs of cigarette smoke produce a synergistic effect on observed chromosome aberration frequencies. In contrast, exposure to reducing agents (ascorbate, cysteine, glutathione) prior to smoke exposure causes a reduction in observed genotoxicity.

Project Dates:
January 1982–January 1984.

Financial Support:
National Research Council of Canada, Associate Committee on Scientific Criteria for Environmental Quality.

0065. BRITISH COLUMBIA CANCER RESEARCH CENTRE, ENVIRONMENTAL CARCINOGENESIS UNIT, 601 West 10th Avenue, Vancouver, British Columbia V5Z 1L3, Canada.

Project Title:
Chemopreventive Trials With Beta-Carotene on Reverse Smokers in the Philippines.

Principal Investigators:
Stich, H.F.; Rosin, M.P.

Objective:
To determine whether beta-carotene can reduce incidence of preneoplastic lesions and carcinomas of the palate and tongue in reverse smokers.

Methods or Approach:
Beta-carotene is being administered twice weekly (180 mg/week) for 6 months. Frequency of exfoliated cells with micronuclei and morphological changes in the leukokeratosis nicotina palati are being used to follow response to beta-carotene treatment.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Chemopreventive trials will be conducted with combinations of beta-carotene, vitamin A, and zinc.

Project Dates:
October 1984–April 1986.
Financial Support:
NCI, Canada.

0066. BRITISH COLUMBIA CANCER RESEARCH CENTRE, ENVIRONMENTAL CARCINOGENESIS UNIT, 601 West 10th Avenue, Vancouver, British Columbia V5Z 1L3, Canada.

Project Title:
Beta-Carotene and Retinol Deficiency in the Buccal Mucosa of Heavy Cigarette Smokers and Alcohol Drinkers.

Principal Investigators:
Stich, H.F.; Dunn, B.P.; Hornby, A.P.
Objective:
To prove or disprove the hypothesis that sensitivity of tissues toward the action of tobacco-related carcinogens depends on level of chemopreventive agents, including beta-carotene and retinol.
Methods or Approach:
Beta-carotene and retinol will be estimated in tissues that are targets for tobacco-related carcinogens and from which carcinomas will actually develop. Exfoliated cells and biopsy material from oral and esophageal mucosa of heavy cigarette smokers and alcohol drinkers will be used to estimate beta-carotene and retinol levels.
Results to Date:
Heavy cigarette smokers and drinkers of alcohol have beta-carotene levels that are approximately 10 percent of those observed in an average Canadian consuming a Western type diet.
Future Plans:
Attempts will be made to separate the effect of cigarette smoking from that of alcohol consumption on levels of beta-carotene in oral mucosa.
Project Dates:
September 1983–September 1986.
Financial Support:
HWC, National Health Research and Development Programme.

0067. BUREAU OF TOBACCO CONTROL AND BIOMETRICS, Laboratory Center for Disease Control, Ottawa, Ontario K1A 0L2, Canada.

Project Title:
Tobacco Related Morbidity and Mortality Estimates for Canada.

Principal Investigator:
Collishaw, N.E.
Objective:
To determine more accurately the estimated annual number of tobacco-related deaths in Canada; estimate patterns of tobacco-related morbidity.
Methods or Approach:
Canadian mortality data were analyzed using tobacco-related estimators developed from national surveys of American death records. Canadian morbidity data were analyzed from special tabulations of the Canada Health Survey 1978-1979.
Results to Date:
The total number of Canadian deaths attributable to tobacco use among persons aged 35 to 84 years was estimated to be between 24,000 and 25,000, or 19 to 20 percent of all deaths in that age group. There are indications that relative risks determined in the 1960s may be lower than the true values for the 1980s, suggesting that these estimates may be conservative. Current and former smokers experienced more self-reported short-term disability than persons who had never smoked, with differences being especially pronounced after age 45. The pattern of steadily increasing disability with age and heavy smoking was more consistent with female than with male smokers.
Future Plans:
Mortality statistics will be monitored to update estimates on tobacco-related deaths.
Project Dates:
1983–continuing.
Financial Support:
HWC.

0068. CANADIAN DEPARTMENT OF NATIONAL HEALTH AND WELFARE, MEDICAL SERVICE BRANCH, Occupational Health Unit, Ottawa, Ontario K1A OL3, Canada.

Project Title:
Impact of a New Smoking Policy on Office Air Quality.

Principal Investigators:
Kirkbride, J.; Lee, H.K.; McKenna, T.A., et al.
Objective:
To evaluate effects of a new smoking policy introduced on one floor of a large modern office building.
Methods or Approach:
Under the new policy, smoking was to be limited to a single, enclosed area that shared the same recirculating type of ventilation system with the rest of the floor. Environmental monitorings were conducted concurrently (on three consecutive working days) on the study floor and on an adjacent control floor in the same building, before and after implementation of the new policy. Hourly levels of respirable suspended particulates (RSP), carbon monoxide, and carbon dioxide were monitored throughout the workday at eight randomly selected sampling sites on each floor. Voluntary questionnaires were circulated to all staff to detect any changes in personal smoking habits over the course of the study.
Results to Date:
After smoking was limited to the staff lounge, there was significant improvement in air quality on the test floor (24 percent reduction in RSP concentration). Measurement of RSP proved to be an appropriate and practical tool for assessing extent of tobacco smoke contamination of indoor air. There were indications that the presence of survey activities alone influenced tobacco consumption and smoking patterns in the survey area.
Project Dates:
December 1984–March 1985.
Financial Support:
HWC.

0069. CANADIAN HEART FOUNDATION, 1200 - One Nicholas Street, Ottawa, Ontario K1N 7B7, Canada.

Project Title:
Smoke-Free Spaces for Kids.

Principal Investigators:
Lauzon, R.R.J.; Gregor, F.
Objective:
To (1) promote nonsmoking as the norm; (2) motivate adults who work with young people to set a nonsmoking example in spaces where children are frequent visitors; (3) create environ-

ments where it is okay not to smoke; and (4) complement and reinforce principles of existing smoking prevention programs.

Methods or Approach:
Individuals who participate in the program (school principals, teachers, youth group leaders, civic officials) will receive awards such as flags, plaques, certificates, and posters.

Results to Date:
Project is in a preliminary phase.

Project Dates:
January 1985–August 1986.

Financial Support:
Canadian Heart Foundation; Canadian Health Promotion Contribution Program; HWC.

0070. CANCER CONTROL AGENCY OF BRITISH COLUMBIA, 2656 Heather Street, Vancouver, British Columbia V5Z 3J3, Canada.

Project Title:
Case-Control Study of Etiological Factors in Head and Neck Cancer.

Principal Investigators:
Elwood, J. M.; Jackson, S.; Flores, A.; Willan, A. R.

Objective:
To evaluate the association of alcohol, tobacco, and occupation to cancer of the head and neck; determine whether such exposures are independent or interactive.

Methods or Approach:
Interviews were conducted with all new patients with these tumors seen at the Cancer Control Agency of British Columbia. This will include about 90 percent of new cases in the province over a 3.5 year period (about 380 cases). The control group will consist of an age- and sex-matched group of patients with other tumors chosen on the basis of lack of association with main exposures, such as breast and gynecological cancer in women, chronic lymphomas and multiple myeloma, and prostatic tumors in men. The interview will provide information on lifetime occupational history and quantification of current and past tobacco and alcohol usage habits.

Results to Date:
Results have been published.

Future Plans:
More detailed analysis of the data is continuing and studies of factors related to early diagnosis are in progress.

Project Dates:
January 1977–December 1983.

Financial Support:
HWC (01027).

Reference:
Elwood, J.M.; Pearson, J.C.G.; Skippen, D.H., et al. "Alcohol, Smoking, Social and Occupational Factors in the Aetiology of Cancer of the Oral Cavity, Pharynx, and Larynx." *International Journal of Cancer* 34(5):603-612, 1984.

0071. CARLETON UNIVERSITY, Department of Psychology, Ottawa, Ontario K1S 4H1, Canada.

Project Title:
Long-Term Effects of Prenatal Exposure to "Soft" Drugs (Including Cigarettes).

Principal Investigator:
Fried, P.A.

Objective:
To investigate the motor, mental, and social development of children from birth to 3 years of age born to mothers who used alcohol, marijuana, and cigarettes during pregnancy.

Methods or Approach:
In a prospective study, pregnant women are interviewed during each trimester remaining in pregnancy. Birth date, nutritional status, neurological assessment, and age-relevant behavior are determined and cognitive tests are administered to infants and children at 4, 9, and 30 days, and at 6, 12, 18, 24, and 36 months.

Results to Date:
In regard to cigarettes, controlling for other drug use and parents' socioeconomic status and nutritional habits, it was found that birth weight was significantly reduced, but gestational age was not. A decrease in gross and fine motor development and in verbal comprehension development was also found.

Project Dates:
April 1980–1985.

Financial Support:
HWC.

0072. CARLETON UNIVERSITY, Department of Psychology, Ottawa, Ontario K1S 5B6, Canada.

Project Title:
Soft Drug Use Prior to and During Pregnancy: A Comparison of Samples Over a Four Year Period.

Principal Investigators:
Fried, P.A.; Innes, K.S.; Barnes, M.V.

Objective:
To determine extent and changing patterns of alcohol, nicotine, and marijuana use in the year before pregnancy and during each trimester of pregnancy among 190 women in the Ottawa Prenatal Prospective Study in 1980-1982; compare results with patterns for women who entered the study in 1978-1979.

Methods or Approach:
Since 1978, pregnant women of unknown "soft" drug usage have been recruited to participate in a prospective investigation involving the Department of Psychology of Carleton University and several hospitals in the city of Ottawa. Subjects volunteered to participate in the Ottawa Prenatal Prospective Study after being informed by their obstetrician or by notices in the public media. The research was described as an investigation of prenatal lifestyle habits and the effects on offspring. Mothers-to-be were interviewed in their homes once during each of the trimesters remaining in their pregnancy at time of entrance into the study.

Results to Date:
There was a striking degree of consistency in the amount of nicotine consumed during prepregnancy and the first trimester between the earlier sample (1978-1979) and women studied in 1980-1982. In both groups, 13 percent of the women consumed an average of 16 mg nicotine/day in the year preceding pregnancy and 8 percent averaged the same amount during the first trimester. However, the proportion of heavy smokers continued to decline among women in the 1980-1982 sample, which was not the case in the earlier cohort.

Project Dates:
March 1987–July 1983.

Financial Support:
HWC.

0073. CARLETON UNIVERSITY, Department of Psychology, Colonel By Drive, Ottawa, Ontario K1S 5B6, Canada.

Project Title:
Soft Drug Use After Pregnancy Compared to Use Before and During Pregnancy.

Principal Investigators:
Fried, P.A.; Barnes, M.V.; Drake, E.R.
Objective:
To study the changing patterns of alcohol, nicotine, and marijuana use of 288 women participating in the Ottawa Prenatal Prospective Study.
Methods or Approach:
In January 1983, a 19-page questionnaire was sent to all women participating in the Ottawa Prenatal Prospective Study whose offspring were at least 1 year of age. Information was gathered retrospectively on pattern and quantity of tobacco use at 1, 6, and 12 months following the birth of the child. Demographic and drug use information for the year preceding pregnancy and for each trimester had been collected as part of interviews conducted during pregnancy.
Results to Date:
Although not as marked as changing alcohol use patterns, nicotine consumption also declined when pregnancy was determined. Cigarette use continued to decline during pregnancy and, unlike alcohol, continued to decrease during the first month after birth. There was only a slight increase in number of heavy smokers at 6 months postpartum. At 1 year, the proportion of women categorized as heavy smokers was at the level observed during the third trimester of pregnancy.
Project Dates:
April 1978–July 1983.
Financial Support:
HWC.

0074. CENTRETOWN COMMUNITY HEALTH CENTRE, 100 Argyle Street, Ottawa, Ontario, Canada.

Project Title:
Healthstyles: A Health Promotion Program.

Principal Investigators:
Black, A.; McDowell, I.; Collishaw, N.E.
Objective:
To promote abandonment and avoidance of unhealthy habits and adoption of health-enhancing behaviors through an intensive 2 1/2-day workshop.
Methods or Approach:
The 4-year community demonstration project uses a quasi-experimental design, matching each of the 630 experimental cases with 2 controls (sample size approximately 1,900). Participants and controls are followed for 18 months. Data are collected (four testing occasions) mainly by questionnaire, although the experimental group is tested for physical fitness at baseline and at 18 months. Specific changes that participants are expected to make include dietary changes, increasing exercise, elimination of smoking, reduction in alcohol consumption, improvement in stress management, and alteration in knowledge and attitudes concerning health. Interventions are tailored to the needs of each participant, and all participants are actively involved in developing personal program objectives and intervention program. Final outcomes will be assessed using the Ontario Provincial health insurance plan data base, to compare physician utilization patterns by experimental and control groups. It is hypothesized that changes will lead to a reduction in physician visits for sickness.
Results to Date:
Preliminary data will be available in 1985; final results will be ready in the fall of 1986.
Future Plans:
When outcome data are available, randomized trials will be conducted on effectiveness of the intervention program in specified groups of patients and high-risk individuals.
Project Dates:
May 1982–November 1986.
Financial Support:
Kellogg Foundation.

0075. CHARLES CAMSELL GENERAL HOSPITAL, FACULTY OF MEDICINE, University of Alberta, Edmonton, Alberta T6G 2G3, Canada.

Project Title:
The Value of the Measurement of Carboxyhemoglobin in Patients With Respiratory Disease.

Principal Investigator:
Herbert, F.A.
Objective:
To determine the disparity between calculated and measured oxygen saturation in smokers.
Methods or Approach:
Patients requiring respiratory evaluation as outpatients or when admitted to ward service are given a special structured history with respect to smoking. Arterial blood gas partial pressures and direct measurements of oxy- and carboxyhemoglobin are performed. In most cases, standard lung function studies are made within a few days.
Results to Date:
Substantial numbers of smokers show a disparity between calculated and measured oxyhemoglobin. In many instances, the disparity is noted in patients who are already quite hypoxic.
Project Dates:
January 1984–January 1986.
Financial Support:
Charles Camsell General Hospital.

0076. CHILDRENS HOSPITAL, 4480 Oak Street, Vancouver, British Columbia V6H 3V4, Canada.

Project Title:
The Effects of Involuntary Smoking on Asthmatic Children.

Principal Investigators:
Murray, A.B.; Morrison, B.J.
Objective:
To determine whether passively inhaled smoke from parents or other household members worsens symptoms in asthmatic children; establish whether smoke increases bronchial reactivity to histamine and decreases spirometric measurements.
Methods or Approach:
The study cohort consists of 94 consecutively referred asthmatic children aged 7 to 17 years. Questions are asked about smoking habits and severity of symptoms. Respiratory function is measured with forced expiratory volume in 1 sec and forced expiratory flow (25-75 percent). A histamine bronchial challenge test is performed on all asymptomatic subjects who have had no recent medication or respiratory infection.
Results to Date:
The is a strong association between presence of cigarette smoke in the home and increased bronchial irritability and decreased spirometric results. There is also a strong correlation between

the log of the number of cigarettes smoked in the home and these changes.

Future Plans:

The effects of passive smoking on rhinitis, middle-ear effusions, and respiratory infections will be studied in addition to further analysis of data.

Project Dates:

October 1983–June 1985.

Financial Support:

British Columbia Lung Association.

0077. DALHOUSIE UNIVERSITY, COMMUNITY REPRODUCTIVE CARE PROGRAM, Department of Pediatrics and Obstetrics, Clinical Research Center, 5849 University Avenue, Halifax, Nova Scotia B3H 4H7, Canada.

Project Title:

Evaluation of Enhanced Community Reproductive Care - A Randomized Clinical Trial of a Community Reproductive Care Program.

Principal Investigator:

Scott, K.E.

Objective:

To (1) determine whether a program of enhanced prenatal care could be accepted and delivered by the medical and public health care delivery systems; (2) determine if apparently healthy pregnant women would accept the preventive program; (3) determine whether a major enhancement of prenatal care could be achieved; (4) determine whether enhancement of care would produce major improvement in maternal environment and personal life; and (5) determine whether such improvement would result in major improvement in perinatal outcome.

Methods or Approach:

A blind clinical trial of enhanced prenatal care involving 11,000 pregnant women was designed, using group allocation after matching on hierarchical scores calculated from previous perinatal outcomes. Enhanced intervention consisted of (1) promotion of optimal antenatal care; (2) serial pregnancy risk assessment (physicians send prenatal records for computer processing and risk assessment, with suggestions for care); (3) referral of the pregnant woman to the Community Health Nurse (CHN) for home visits; (4) data collection on medical or pregnancy disease, previous pregnancies, prenatal care, prenatal class attendance, exercise, prenatal weight and height, nutrition, personal support, food finances, stress, and cigarette, alcohol, and drug consumption; and (5) counseling on areas of concern, particularly on smoking cessation.

Results to Date:

Compliance was 89 percent for physicians, 93 percent for CHNs, and 97 percent among mothers. In the enhanced care cohort, 62 percent were visited at home. Smoking was associated with low birth weight in two-thirds of infants weighing <2,500 g, and was probably causal in half, masking all other factors. In nonsmokers, inadequate nutrition, lack of exercise, and insufficient food finances were important factors. Lifestyle was suboptimal in 79 percent and nutrition was inadequate in 43 percent, 35 percent were smokers, 24 percent did not attend prenatal classes, 16 percent did not exercise, 9 percent had inadequate food finances, and 5 percent consumed alcohol. With optimal lifestyle (35 percent) low birth weight was 1.6 percent compared with 5.2 percent for suboptimal lifestyle. Lifestyle was the main factor in 59 percent of low birth weight infants. Results suggest that there is an upward shift in birth weight and a declining incidence of low birth weight. Hospital care savings would be 1.2 million, and 2.5 million could be saved by eliminating all excess low birth weight outcomes (not including preventable mental handicap).

Future Plans:

Further data analysis and linking of several other sources of data are planned, which will include 2,082 questionnaire returns from both sides of the trial, 2,393 prenatal records for weight gain and fundal height curve studies, and hospital admission and separation data from the 11,000 pregnancies. Selected aspects of the trial are now being implemented in the previous control areas, and results will be evaluated.

Project Dates:

May 1980–March 1983.

Financial Support:

Dalhousie University, Canada; National Health Research and Development Program, Canada; Nova Scotia Department of Health; Hospital for Sick Children Foundation, Canada.

0078. DEFENCE AND CIVIL INSTITUTE OF ENVIRONMENTAL MEDICINE, Downsview, Ontario M3M 3B9, Canada.

Project Title:

The Relationship Between Aerobic Fitness and Certain Cardiovascular Risk Factors.

Principal Investigators:

Brown, T.E.; Myles, W.S.; Allen, C.L.

Objective:

To investigate the relationship between aerobic fitness and incidence of risk factors related to cardiovascular disease (CVD) in Canadian servicemen 18 to 50 years of age.

Methods or Approach:

Aerobic power was predicted from heart rate measured during submaximal bicycle exercise. Serum cholesterol, serum triglycerides, blood pressure, and body fat were measured, and incidence of cigarette smoking was obtained by questionnaire. Subjects were divided into three age groups and subdivided into four fitness categories.

Results to Date:

Incidence of cigarette smoking was inversely related to fitness category only in those ≥ 30 years of age, although incidence of smoking declined slightly as fitness category improved. There is some evidence that individuals, once embarked on an exercise program, modify other lifestyle habits that adversely affect health; however, data concerning smoking habits provide conflicting evidence. Although it is well known that cigarette smoking is a major CVD risk factor, the incidence in the youngest age group was unrelated to fitness, and even in the two older age groups, there was no way of knowing how many found cigarette smoking incompatible with fitness. An inverse relationship was demonstrated between fitness category and mean values for all measured risk factors. Although this relationship was most evident in older subjects, it is significant that it was also present in men under 30 years of age. It is suggested that participation in a program to improve physical fitness may lead the individual to modify other lifestyle components.

Reference:

Brown, T.E.; Myles, E.S.; Allen, C.L. "The Relationship Between Aerobic Fitness and Certain Cardiovascular Risk Factors." *Aviation, Space, and Environmental Medicine* 54(6):543-547. June 1983.

0079. GIPPSLAND INSTITUTE OF ADVANCED EDUCATION, Switchback Road, Churchill, Victoria 3842, Canada.

Project Title:
An Evaluation of Latrobe Valley Community Smoking Control Project (LVCSCP).

Principal Investigator:
Fraser, C.O.
Objective:
To (1) measure changes in school-age and general population smoking rates during the first 4 years of the LVCSCP; (2) measure awareness of LVCSCP in both the general community and specific groups; (3) identify specific programs and promotional activities provided by the LVCSCP; and (4) evaluate operation of the LVCSCP committee, its relations with other community groups, inputs of members, and degree of agreement on how to achieve objectives.
Methods or Approach:
The five-step program will (1) prepare and pilot-test measures for evaluating peer leadership programs and prepare for school population survey (3 months); (2) conduct school population survey (pretest schools involved in specific programs and continue monitoring operation of programs), (3 months); (3) conduct followup of specific schools, including saliva continine followup, and analyze data from school population survey (3 months); (4) analyze and evaluate specific school programs and conduct second followup after 1 year (6 months); and (5) prepare final report (3 months).
Results to Date:
When available, results will be presented at health education conferences and prepared for publication. Copies will be distributed to other researchers in the field, and will be available on request.
Project Dates:
June 1984–June 1985.
Financial Support:
Commonwealth Department of Health (HSR 215).

0080. HEALTH AND WELFARE CANADA, Bureau of Tobacco Control and Biometrics, Laboratory Centre for Disease Control, Ottawa K1A 0L2, Canada.

Project Title:
Trends in Tobacco Consumption.

Principal Investigator:
Collishaw, N.E.
Objective:
To determine trends in estimated tobacco consumption by Canadians; investigate the relationship between tobacco prices and consumption over and consumption and self-reported tobacco use and morbidity.
Methods or Approach:
Existing data sets are reanalyzed and reconciled to yield more accurate estimates of tobacco consumption trends in Canada. Tobacco sales reported to Statistics Canada and self-report tobacco use data from annual smoking surveys and the 1978-1979 Canada Health Survey are utilized.
Results to Date:
Cigarette consumption in Canada remained constant on a per capita basis at about 10 cigarettes/day for persons aged 15 or older; however, average consumption of smokers increased from 24 cigarettes/day in 1975 to 27 cigarettes/day in 1981. Over the same period, average cigarette weight and sales-weighed tar declined. Weight of tobacco consumed per smoker has increased modestly since 1975, but daily tar consumption per smoker declined over the same period, for both men and women. When self-report data were reconciled with tobacco sales reports, the former were found to have increasingly underestimated apparent consumption of tobacco over time. Price elasticities for tobacco in various countries range from -0.2 to -0.8, and estimates of price elasticity for Canada fall in this range.
Project Dates:
January 1982–continuing.
Financial Support:
HWC.

0081. HEALTH PROMOTION DIRECTORATE, 831 Portage Avenue, 4th Floor, Winnipeg, Manitoba R3G 0N6, Canada.

Project Title:
Baseline Data on Smoking Behavior of Youth (Grade 3 - 12).

Principal Investigator:
Manfreda, J.
Objective:
To (1) collect data on smoking behavior of school-aged children in Manitoba; (2) conduct update on data every 2 years; and (3) evaluate impact of smoking prevention programs.
Methods or Approach:
A questionnaire was completed by schoolchildren in grades 3 to 12. Approximately 10 percent of Manitoba schoolchildren answered the questionnaire. Classes were randomly selected.
Results to Date:
Results are not yet available.
Future Plans:
Data will be used for program planning and to evaluate impact of prevention/cessation programs.
Project Dates:
January 1985–March 1985.
Financial Support:
Health Promotion Directorate, Manitoba.

0082. HEALTH PROMOTION DIRECTORATE, 831 Portage Avenue, 4th Floor, Winnipeg, Manitoba R3G 0N6, Canada.

Project Title:
"It's for Me and You, Baby"; An Audio Visual Slide Presentation Dealing With the Hazard of Smoking, Drinking, and Use of Medication During Pregnancy.

Principal Investigator:
Chan, T.V.
Objective:
To develop an audiovisual educational resource to be used in early-bird and refresher prenatal classes.
Methods or Approach:
The audiovisual slide presentation was developed collaboratively with prenatal instructors and prenatal clients. The presentation will be pilot-tested in spring 1985.
Results to Date:
Project is in a preliminary phase.
Project Dates:
September 1984–February 1985.
Financial Support:
Health Promotion Directorate, Manitoba.

0083. HEALTH PROMOTION DIRECTORATE, 831 Portage Avenue, 4th Floor, Winnipeg, Manitoba R3G 0N6, Canada.

Project Title:
Peer Assisted Smoking Prevention Pilot Project.

Principal Investigator:
Health and Welfare Canada.
Objective:
To (1) measure smoking behavior of youth aged 11 to 13 in the Peer Assisted Smoking Prevention Pilot Project (PASP); (2) pilot the PASP project in Manitoba schools; (3) evaluate project material from the perspective of students, parents, and teachers; and (4) determine strengths and weaknesses of PASP.
Methods or Approach:
Smoking behavior of students in seventh grade is measured. Self-report questionnaires are completed at beginning and end of the project. Core lessons and booster lessons are administered throughout the year. Evaluation of the pilot project will be conducted in September 1985.
Results to Date:
Project is in a preliminary phase.
Future Plans:
The project will be implemented throughout Canada in 1986, and may be used in fifth grade (ages 9 to 11) if findings show that children experiment with smoking before seventh grade.
Project Dates:
September 1984–September 1985.
Financial Support:
Health Promotion Directorate, Manitoba.

0084. HOPITAL DU SACRE-COEUR, Pulmonary Division, 5400 Gouin Boulevard West, Montreal, Quebec H4J 1C5, Canada.

Project Title:
Occupational Asthma in Snow Crab Processing Workers.

Principal Investigators:
Cartier, A.; Malo, J.-L.
Objective:
To conduct an epidemiological survey of prevalence of occupational asthma in snow crab processing workers.
Methods or Approach:
Prevalence was studied in two snow crab processing industries in operation since 1980. Before the 1982 season, 303 (of 313) employees were investigated by questionnaire, skin prick tests with common allergens, crab and crab-boiling water extracts, and spirometry. All workers were interviewed on several occasions during the season about any occurrence or exacerbation of respiratory symptoms, rhinoconjunctivitis, and urticaria.
Results to Date:
Diagnosis was confirmed in 46 workers (15.6 percent), including 33 of 64 subjects with a history highly suggestive of occupational asthma in previous seasons, by (1) specific inhalation challenges in 33 subjects and/or (2) a combination of monitoring of peak expiratory flow rates and significant changes in bronchial rseponsiveness to histamine and spirometry after reappearance of symptoms on return to work. Positive skin tests to crab and, to a lesser degree, smoking history, but not atopy were related to presence of occupational asthma. It is speculated that smoking, by altering bronchial permeability, could allow penetration of the antigen to effector cells. A high prevalence of rhinoconjunctivitis and urticaria was also documented in affected individuals.
Financial Support:
Departement de Sante Communautaire, Gaspe, Canada.
Reference:
Cartier, A.; Malo. J.-L.; Forest, F., et al. "Occupational Asthma in Snow Crab-Processing Workers." *Journal of Allergy and Clinical Immunology* 74(3, Part 1):261-269, September 1984.

0085. MCGILL UNIVERSITY, Department of Anthropology, Stephen Leacock Building, 855 Sherbrooke Street West, Montreal, Quebec H2X 1X8, Canada.

Project Title:
The Anthropology of Nicotiana: Origins and Use of Tobacco Among Aboriginal Cultures.

Principal Investigator:
Von Gernet, A.D.
Objective:
To create an extensive literature data bank for the first interdisciplinary study of tobacco use among prehistoric and modern, nonwestern peoples; scrutinize relevant information more carefully by circumventing many of the biases inherent in studies produced by health professionals or tobacco industries.
Methods or Approach:
Compilation of the data bank involves a 3-year search and perusal of relevant literature produced by a number of disciplines including archeology, ethnobotany, ethnohistory, ethnology, folklore studies, history, linguistics, medical anthropology, and psychopharmacology. Although many indigenous societies throughout the world quickly adopted tobacco use after 1600, by far the greatest number of references in anthropological literature come from North and South America and much of the study will concentrate on these areas. Copies of articles and books exclusively on, or containing information about, aboriginal tobacco use will be obtained for the data bank. Information will be extracted and synthesized so that a broader perspective of human use of *Nicotiana* will emerge.
Results to Date:
Over 40,000 articles, books, and extracts have been collected and are currently being organized to facilitate information access. Preliminary analysis provide the following tentative conclusions: (1) prehistoric and early historic use of tobacco in the New World occurred in both sacred and secular settings, and was far more widespread than at any point in the history of industrialized societies; (2) proportions of active ingredients (such as nicotine or harmala alkaloids) in native tobacco species often greatly exceeded those found in modern cigarettes; (3) tobacco was employed in production of altered states of consciousness and must be viewed in the general context of the New World indigenous psychotropic drug complex; and (4) evolution of tobacco use was linked to its role as a chemical reinforcer of the psychic states valued in aboriginal ideologies.
Future Plans:
A complete bibliography and index will be computerized and made available to interested researchers.
Project Dates:
August 1981–August 1987.
Financial Support:
Social Sciences and Humanities Research Council of Canada.

0086. MCGILL UNIVERSITY, SCHOOL OF OCCUPATIONAL HEALTH, 1130 Pine Avenue West, Montreal, Quebec H3A 1A3, Canada.

Project Title:
Reproductive Effects of Occupational Exposure of Women to Low Doses of Metallic Mercury.

Principal Investigators:
Theriault, G.; De Guire, L.
Objective:
To observe the reproductive effects of occupational exposure of women to low doses of metallic mercury; determine whether occupational exposure to mercury is related to problems for the embryo or fetus of mothers exposed during pregnancy, menstrual problems, or infertility in exposed women.
Methods or Approach:
Female workers (current and former) of three fluorescent plants in Canada will be divided into two groups: exposed to metallic mercury and nonexposed. Approximately 1,000 women will be studied. Reproductive history (pregnancies, menstrual cycle, fertility), occupational history, socioeconomic status, medical history, tobacco, alcohol, and drug consumption, and health status of children will be assessed by self-administered questionnaires. Exposure will be established by environmental data available from a governmental agency. Frequency of low birth weight and spontaneous abortion in the two groups of women will be compared.
Results to Date:
Results are not yet available.
Project Dates:
1981–1986.

0087. MCGILL UNIVERSITY, SCHOOL OF OCCUPATIONAL HEALTH, 1130 Pine Avenue West, Montreal, Quebec H3A 1A3, Canada.

Project Title:
Cardiac Ischemic Disease Among Workers in Aluminium Industry.

Principal Investigators:
Tremblay, C.; Theriault, G.
Objective:
To determine whether environmental and occupational exposure can explain the excess of ischemic heart disease; examine the synergistic relationship between tobacco and occupational exposure to chemicals.
Methods or Approach:
In this case–control study, 323 ischemic heart disease patients were identified; two controls were selected for each case, matched for age, hiring date, and length of employment. Occupational history and physical and chemical exposures will be compared between the groups and an odds ratio will be calculated.
Results to Date:
Results are not yet available.
Project Dates:
January 1984–June 1985.
Financial Support:
Institut de Recherche en Sante et en Securite du Travail du Quebec.

0088. MCGILL UNIVERSITY, Department of Pathology, 3775 University Street, Montreal, Quebec H3A 2B4, Canada.

Project Title:
Nicotine Induced Fetal Lung Changes.

Principal Investigators:
Wang, N.-S.; Chen, M.-F.
Objective:
To determine the relationship between human fetal lung changes and maternal smoking during pregnancy.
Methods or Approach:
Although more than 50 cases have been collected, only 16 specimens of perinatal lungs obtained at autopsy were found to be usable; 10 had a positive history of smoking during pregnancy (group 1) and 6 had a negative history (group 2). One or both lungs from each case were studied by light microscopy, transmission electron microscopy, and scanning electron microscopy.
Results to Date:
Owing to the small numbers and differing gestational ages and pathological diagnoses, statistical analyses have not been made; however, results strongly suggest that (1) there is no change in the alveolar mean linear intercept length between the two groups; (2) there is a decrease in the alveolar surface area (smaller lungs) with an increase in the number of cigarettes smoked; and (3) there is an increased number with larger mean diameter of neuroepithelial bodies (NEBs) in group 1 compared with group 2.
Future Plans:
Studies will incorporate immunocytochemistry to delineate NEB using neuron-specific enolase, serotonin, and bombesin as markers, and will take into consideration the number of cigarettes smoked. Findings should clarify the pathogenetic mechanisms of lung NEB changes and delineate the degree of dose-dependent risk associated with maternal smoking during pregnancy.
Project Dates:
July 1983–June 1985.
Financial Support:
Quebec Lung Association.
References:
(1) Wang, N.S.; Schraufnagel, D.E.; Chen, M.F. "The Effect of Maternal Oral Intake of Nicotine on the Growth and Maturation of Fetal and Baby Mouse Lungs." *Lung* 161:27-38, 1983. (2) Wang, N.S.; Schraufnagel, D.E.; Chen, M.F. "The Effect of Maternal Oral Intake of Nicotine on the Lung of the Offspring in Mice." *American Review of Respiratory Disease* 123(Part 2):149, 1981. (3) Chen, M.F.; Diotallevi, G.; Kimizuka, G., et al. "A Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) Study of Baby Rabbit Lungs Following Maternal Injection of Nicotine." *Federation Proceedings* 43:880, 1984. (4) Kimizuka, G.; Yoshizaki, K.; De Bock, V., et al. "The Effect of Maternal Injection of Nicotine on the NEB and Serotonin Levels of Fetal and Baby Rabbit Lungs." *American Review of Respiratory Disease* 129: A172, 1984. (5) Wang, N.S.; Chen, M.F.; Schraufnagel, D.E., et al. "Cumulative Scanning Electron Microscopic Changes in Baby Mouse Lungs Following Prenatal and Postnatal Exposures to Nicotine." *Journal of Pathology* 144:89-100, 1984.

0089. MCMASTER UNIVERSITY, FACULTY OF HEALTH SCIENCES, H.S.C. 2041, 1200 Main Street West, Hamilton, Ontario L8N 3Z5, Canada.

Project Title:
Family Practice Smoking Cessation Project.

Principal Investigators:
Wilson, D.M.C.; Best, J.A.; Gilbert, J.R., et al.
Objective:
To (1) evaluate the impact of procedures designed to improve patient compliance with a nicotine chewing gum (NCG) regimen compared with NCG prescription alone; (2) identify factors that affect physician compliance with a recommended NCG prescription protocol; (3) develop procedures designed to improve physician compliance; and (4) describe the typical smoking cessation process following NCG prescription in each experimental condition.
Methods or Approach:
A randomized clinical trial will compare 25 family physicians who offer a NCG prescription to a representative sample of adult patients who smoke with 25 physicians who are trained to use compliance enhancement procedures when prescribing the gum. The three-group design will also compare the two treatment groups with a group of 25 physicians who will provide usual care. The strategies, which are simple enough to be implemented by busy physicians and effective enough to reduce major compliance problems found with NCG, will be evaluated. Each physician will recruit 30 smokers. Smoking cessation rates will be determined at 1-year followup by saliva cotinine tests.
Results to Date:
Physician orientation and training is scheduled for early 1985; recruitment of smokers will follow.
Future Plans:
Data will be used to design future studies that will investigate both patient and physician compliance.
Project Dates:
October 1984–May 1987.
Financial Support:
NCI (1R01CA38334-01).

0090. MONTREAL GENERAL HOSPITAL, Department of Community Health, 1597 Pine Avenue West, Montreal, Quebec H3G 1B3, Canada.

Project Title:
Cigarette Smoking, Lung Cancer, and Canadian Women.

Principal Investigators:
L'Abbe, K.A.; Hoey, J.R.
Objective:
To (1) investigate recent trends in smoking habits and lung cancer mortality of Canadian women; (2) study trends in tobacco advertising, sales, and relationship to tobacco consumption patterns; and (3) investigate apparent dependence of number of antismoking articles in women's magazines on revenues from tobacco advertisements in the magazines.
Methods or Approach:
The epidemiology of lung cancer and proportion attributed to cigarette smoking were reviewed. Smoking patterns by age and sex were taken from the Canada Health Survey and the Labour Force Survey. Public policy literature on smoking was also reviewed. Through personal communications and material published by the tobacco industry, revenue generated from tobacco sales and amount spent on advertising over a 10-year period were obtained. The frequency of articles on smoking and health and how they were related to whether or not a magazine accepted cigarette advertising was obtained by reviewing several women's magazines for a 15-year period.
Results to Date:
Lung cancer is overtaking breast cancer as the leading cause of cancer mortality in women; 60 percent of lung cancers are attributable to cigarette smoking. Although there has been a large decline in the percentage of male smokers, the decline is very small in women, who are also smoking more cigarettes/day. The tobacco industry spent over 100 million dollars on advertising in Canada in 1983. Only magazines that do not accept cigarette advertisements have increased coverage of the hazards of smoking. It is recommended that a ban be placed on all forms of tobacco advertising.
Project Dates:
November 1983–June 1984.
Financial Support:
HWC; Ministry of Social Affairs of Quebec.
Reference:
L'Abbe, K.A.; Hoey, J.R. "Cigarette Smoking, Lung Cancer and Canadian Women." *Canadian Medical Association Journal* 130:1539-1540, June 15, 1984.

0091. NATIONAL CANCER INSTITUTE OF CANADA, UNIVERSITY OF TORONTO, Department of Preventive Medicine and Biostatistics, Medical Sciences Building, Toronto, Ontario M5S 1A8, Canada.

Project Title:
Epidemiological Study of Bladder Cancer.

Principal Investigators:
Miller, A.B.; Howe, G.R.; Burch, J.D., et al.
Objective:
To (1) evaluate further the occupational causes of bladder cancer; (2) clarify the role of tobacco smoking in the etiology of bladder cancer, particularly the differential effect of filter and regular cigarette smoking and the effect of pipe smoking; (3) clarify the role of artificial sweeteners in the etiology of bladder cancer and particularly the temporal relationships of the association; (4) clarify the role of coffee consumption and its components, especially the role of instant and regular coffee in males and females; (5) study the association of bladder cancer with nonpublic water supplies; and (6) collect data on the possible association of hair dye use and bladder cancer.
Methods or Approach:
The study is a population-based case–control study with case and control acquisition from Alberta and southern Ontario. Data on past events and exposures were obtained from 848 cases and 782 controls by means of a detailed questionnaire. The cases were patients with bladder cancer newly diagnosed from April 1, 1979, through March 31, 1982. Controls were matched with cases on age and sex and were randomly selected from the municipality in which the cases lived.
Results to Date:
Analysis of data is being performed.
Project Dates:
April 1979–1984.
Financial Support:
NCI, Canada.

0092. NATIONAL CANCER INSTITUTE OF CANADA, UNIVERSITY OF TORONTO, Faculty of Medicine, McMurrich Building, Toronto, Ontario M5S 1A8, Canada.

Project Title:
Study of the Epidemiology of Lung Cancer in Women.

Principal Investigators:
Miller, A.B.; Jain, M.
Objective:
To (1) assess the extent to which lung cancer in women is attributable to cigarette smoking and the risk of smoking different types of cigarettes; (2) assess, in women and in an age-

matched series of men, a possible protective effect of foods containing Vitamin A; and (3) attempt to assess, in women, the contribution of other risk factors in the etiology of lung cancer, including occupation, passive smoking, and exposure to other known or unknown environmental factors.

Methods or Approach:
All newly diagnosed cases of female lung cancer in metropolitan Toronto together with a matched series of male lung cancer cases are being included. Each case is matched against a population control by age, sex, and borough of residence. The study therefore takes the form of two identically planned case–control studies. Information is collected by means of personal interviews on education, smoking, residence, occupation, some dietary factors, and ethnicity. In 1984, additional questions were added relevant to radon daughter accumulation in homes. By November 1984, 385 female and 325 male cases and 297 female and 248 male controls had been interviewed. Relative risk ratios and attributable risk percentage will be calculated for different variables, controlling for confounding variables.

Results to Date:
Interviews are still being conducted.

Project Dates:
April 1981–March 1985.

Financial Support:
NCI, Canada.

0093. NATIONAL CANCER INSTITUTE OF CANADA, UNIVERSITY OF TORONTO, Epidemiology Unit, McMurrich Building, Toronto, Ontario M5S 1A8, Canada.

Project Title:
Epidemiological Study of Cerebral Tumors in Adults.

Principal Investigators:
Burch, J.D.; Howe, G.R.; Miller, A.B.

Objective:
To investigate the association of urban/rural differences, occupation, family associations, ionizing radiation, brain trauma, and specific chemical carcinogens with the incidence of cerebral tumors in adults.

Methods or Approach:
The study tests the hypotheses that cerebral tumors are associated with specific occupations (farming, rubber industry, plastics industry), family history of brain tumor, and exposure to nitrosamines, especially through drinking water and preservative-containing meats and meat products. A number of questions were also asked of respondents relating to additional environmental factors such as smoking and alcohol consumption. Data on past events and exposures was obtained from 251 cases and 233 hospital controls through personal interviews in the respondents' homes using proxy respondents for dead or incapacitated cases, and appropriate proxy controls. Case and control acquisition was restricted to the metropolitan Toronto and fringe areas and included incident cases with defined histology for the 4-year period from January 1, 1977 through December 31, 1981.

Results to Date:
Analysis of data is being performed.

Project Dates:
1979–1984.

Financial Support:
NCI, Canada.

0094. NOTRE-DAME HOSPITAL, Respiration Division, 1560 Sherbrooke Street East, Montreal, Quebec, Canada.

Project Title:
Effect of Smoking on Regional Lung Function in Sarcoidosis.

Principal Investigators:
Dutton, R.E.; Renzi, P.M.; Lopez-Majano, V., et al.

Objective:
To determine whether the regional distribution and severity of lung disease in patients with sarcoidosis is influenced by smoking.

Methods or Approach:
Patients with pulmonary sarcoidosis proved by biopsy are grouped according to current smoking habits into smokers and nonsmokers. Regional lung function is determined by regional analysis of chest radiographs and by xenon^{133} methods for determination of regional lung ventilation, volume, and lung perfusion. Global lung function studies are also obtained. Closing volume, which reflects regional differences in airway closure, is also measured by the xenon^{133} bolus technique.

Results to Date:
In 7 smokers and 13 nonsmokers, the xenon method revealed a high incidence of reduced ventilation and lung volume in the upper lobes of the lung, whereas the distribution of perfusion to these lobes was normal. In contrast to the lack of significant differences between smokers and nonsmokers for abnormal regional lung function in the upper lobes, smokers had a significantly higher regional volume and significantly lower regional perfusion of the lower lobes than nonsmokers. All smokers had a xenon^{133} closing volume, expressed as a ratio to vital capacity, that was abnormally high (>120 percent predicted). The result of changes in smokers is a loss of normal regional lung volume gradient from top to bottom in the lungs. In smokers, impaired blood flow to hyperinflated lower lobes causes redistribution of pulmonary blood flow to diseased middle and upper zones of the lungs.

Future Plans:
Future studies are planned in patients with other causes of pulmonary fibrosis.

Project Dates:
July 1982–continuing.

Financial Support:
NIGMS (GM 15426); NHLBI (HL 12564); Notre Dame Foundation (6315).

Reference:
Dutton, R.E.; Renzi, P.M.; Lopex-Majano, V., et al. "Total and Regional Lung Function in Sarcoidosis: Smokers Versus Nonsmokers." *Annals of the New York Academy of Science* (In press).

0095. NOTRE-DAME HOSPITAL, RESPIRATORY SERVICE, 1560 Sherbrooke Street East, Montreal, Quebec H2L 4K8, Canada.

Project Title:
Effect of Smoking on Total and Regional Lung Function in Sarcoidosis.

Principal Investigators:
Renzi, G.D.; Renzi, P.M.; Dutton, R.E., et al.

Objective:
To evaluate site and severity of pulmonary involvement by means of total and regional lung function tests; compare pathophysiological changes of sarcoidosis alone in nonsmokers with pathophysiological changes of sarcoidosis in smokers who

have an added danger of developing obstructive pulmonary disease due to smoke inhalation.

Methods or Approach:

Following staging of disease by radiological criteria, patients with proven sarcoidosis are grouped into smokers and nonsmokers. Pulmonary function tests are used to identify location of airway disease in small or large airways of the lung. Regional distribution of ventilation and perfusion and of lung volumes are performed by xenon inhalation and intravenous injection of xenon, respectively. Closing volume is performed by the bolus technique.

Results to Date:

Global lung function tests in the 13 nonsmokers and 7 smokers studied showed significant abnormalities in both groups for forced expiratory flow at 25 to 75 percent vital capacity and airway resistance, signifying obstructive lung disease. Total lung capacity was increased in smokers ($p<0.02$), as was residual volume in percent of predicted ($p<0.005$). Regional distribution of ventilation was comparable in smokers and nonsmokers, but incidence of abnormal regional lung volumes was significantly higher in smokers ($p<0.05$). All smokers had regional closing volume/vital capacity in percent of predicted <120 percent. Smokers had hyperinflation of the lower lobes secondary to effect of smoking on small airways, resulting in airway closure. Smoking and sarcoidosis have synergistic effects that induce a high incidence of airway abnormalities.

Future Plans:

The study will be extended for long-term followup.

Project Dates:

July 1980–July 1987.

Financial Support:

USPHS (HL 12564; GM 15426); Notre-Dame Foundation, Montreal.

0096. ONTARIO MINISTRY OF LABOUR, 400 University Avenue, Toronto, Ontario, M7A 1T7, Canada.

Project Title:

Dose–Response Relationships for Asbestos Disease.

Principal Investigator:

Finkelstein, M.M.

Objective:

To investigate the quantitative relationships between exposure to asbestos dust and the risks of development of respiratory abnormalities and malignant disease.

Methods or Approach:

Historical prospective cohort studies are being used to follow up employees of an Ontario asbestos cement factory. End points are mortality, radiographic abnormalities, and pulmonary function abnormalities. Smoking histories were obtained by questionnaire or during routine medical surveillance.

Results to Date:

Results to date indicate that smokers are at increased risk of radiographic and pulmonary function abnormalities.

Project Dates:

December 1978–continuing.

Financial Support:

Ontario Ministry of Labour.

0097. ONTARIO MINISTRY OF LABOUR, 400 University Avenue, 8th Floor, Toronto, Ontario M7A 1T7, Canada.

Project Title:

Ontario Miners Mortality Study.

Principal Investigators:

Muller, J.; Suranyi, G.; Kusiak, R., et al.

Objective:

To (1) evaluate the risk of dying in nonuranium miners by cause and by ore mined; (2) determine dose–time response function for cancers of the trachea, bronchus, and lung from exposure to short-lived daughters of radon-222; (3) evaluate effect of other contaminants in present or former work environment that might affect lung cancer risk in uranium miners; and (4) determine possible differences in relative frequencies of lung cancer by cell type in various groups of miners.

Methods or Approach:

A detailed work history was compiled for all types of miners (gold miners, nickel miners, iron ore miners, other ore miners, miners with varied experience, and uranium miners). For uranium miners, a detailed history of exposure to short-lived daughters of radon-222 was produced for each man. A death search for the total cohort (50,201 men) was carried out in cooperation with Statistics Canada over the period from January 1, 1955, to December 1977. For uranium miners, the search was updated to December 31, 1981.

Results to Date:

Study results have been published.

Future Plans:

The effect of smoking and occupational exposure on lung cancer risk by cell type is being investigated in various groups of miners. The effect of smoking on lung cancer risk by cell type is also being studied in the Ontario population to correct for possible differences in smoking habits in miners and nonminers.

Project Dates:

1980–February 1986.

Financial Support:

Ontario Ministry of Labour; Workers' Compensation Board of Ontario; Atomic Energy Control Board of Canada.

Reference:

Ontario, Ministry of Labour. "The Study of Mortality of Ontario Miners 1955-1977, Part 1." May 1983.

0098. ROYAL OTTAWA HOSPITAL, 1145 Carling Avenue, Ottawa, Ontario K1Z 7K4, Canada.

Project Title:

Tobacco Smoking as a Coping Mechanism in Psychiatric Patients.

Principal Investigator:

Knott, V.J.

Objective:

To delineate motivational factors underlying tobacco use in psychiatric patients.

Methods or Approach:

Research methods include (1) documentation of smoking characteristics of patients via questionnaires and behavioral analysis of smoking; (2) analysis of biochemical indices of smoking behavior; and (3) analysis of physiological affects of smoking and smoking abstinence. Study designs will involve comparison of various patient groups (schizophrenics, depressives, those with anxiety disorders) with controls and will also document within-group changes, such as variations in the measures across treatment.

Results to Date:

Project is in a preliminary phase.

0099. SIMON FRASER UNIVERSITY, Department of Computing Science, Burnaby, British Columbia V5A 1S6, Canada.

Project Title:
Health and Comfort in Nine Office Buildings.

Principal Investigators:
Sterling, T.D.; Sterling, E.M.
Objective:
To compare prevalence of complaints of discomfort or of symptoms in offices where smoking is permitted, restricted, or prohibited.
Methods or Approach:
Detailed health and environment questionnaires were received from approximately 1,100 members of a union of office professional employees. Information was collected on environmental conditions (air movement, lighting, odors), lighting conditions (fluorescent and window lighting), health-related symptoms (headaches, dizziness, fatigue, sleepiness), lifestyle and personal factors (including smoking), and stress factors. Groups were identified with regard to smoking habit and office smoking restrictions. Employees rated working environments as good, average, or fair.
Results to Date:
Good ventilation conditions were reported by 11.7 percent of 128 nonsmokers working where smoking was permitted, compared with 10.8 percent to 11.4 percent of nonsmokers working in smoking-restricted offices. Ventilation was rated poor by 32 percent of nonsmokers in smoking-permitted offices compared with 23.3 to 28.6 percent of nonsmokers in smoking-restricted offices. Employees working where smoking was permitted reported substantially less stress than those in smoking-restricted offices. Fewer reports of eye, nose, and throat irritations were reported in smoking-restricted offices, but fewer headaches were reported in nonrestricted (51.6 percent of reports) compared with restricted (75 percent) offices. No objective evidence was found that health-related complaints differed between locations with or without smoking restrictions.
Reference:
Sterling, T.D.; Sterling, E.M. "Environmental Tobacco Smoke. 1.2. Investigations on the Effect of Regulating Smoking on Levels of Indoor Pollution and on the Perception of Health and Comfort of Office Workers." *European Journal of Respiratory Diseases* 65(Supplement 133):17-32, 1984.

0100. SIMON FRASER UNIVERSITY, Department of Computing Science, Burnaby, British Columbia V5A 1S6, Canada.

Project Title:
Studies on Indoor Air Pollution.

Principal Investigators:
Sterling, T.D.; Sterling, E.M.
Objective:
To (1) review pollutant levels reported for 111 buildings receiving persistent complaints; (2) compare data with that of 32 buildings with no complaints; and (3) compare pollutant levels in buildings based on rules permitting or restricting smoking.
Methods or Approach:
Adequate measurements were available on 12 suspected indoor pollutants possibly related to smoking and were converted to common units of measurement. Pollutants included aldehydes, amines, aromatic hydrocarbons, carbon dioxide, carbon monoxide, formaldehyde, hydrocarbons, nitrogen oxides, nitrogen dioxide, ozone, particulates, and sulfur dioxide.
Results to Date:
Levels of carbon monoxide and particulates were not significantly different between buildings receiving complaints and those without complaints, regardless of level of smoking restrictions. Average level of suspended particulates was 0.028 mg/m^3 in buildings with complaints and 0.037 mg/m^3 in buildings without complaints (all buildings without smoking restrictions). No differences were found in average values of pollutants measured in buildings with and without smoking restrictions, and none between buildings with health-related complaints and those without such complaints.
Reference:
Sterling, T.D.; Sterling, E.M. "Environmental Tobacco Smoke. 1.2. Investigations on the Effect of Regulating Smoking on Levels of Indoor Pollution and on the Perception of Health and Comfort of Office Workers." *European Journal of Respiratory Diseases* 65(Supplement 133):17-32, 1984.

0101. ST. PAUL'S HOSPITAL, U.B.C. Pulmonary Research Laboratory, Vancouver, British Columbia V6Z 1Y6, Canada.

Project Title:
Nonspecific Airway Reactivity in Cigarette Smokers.

Principal Investigators:
Mullen, J.B.M.; Wright, J.L.; Hogg, J.C., et al.
Objective:
To examine relationship of cigarette smoking, starting airway caliber, and airway pathology to nonspecific airway reactivity.
Methods or Approach:
Cigarette smokers will perform methacholine inhalation challenge tests prior to lung surgery for bronchogenic carcinoma. Patients will also undergo preoperative pulmonary function tests. Resected specimens will be graded for large and small airway pathology and emphysema.
Results to Date:
Data suggest that cigarette smoking, starting airway caliber, and airway inflammation are associated with nonspecific airway reactivity and that each exerts an effect on airway reactivity that is not dependent on the contribution of the other two factors.
Future Plans:
The relationship of airway inflammation to chronic bronchitis and effect of smoking status on airway structure will be examined.
Project Dates:
September 1982–September 1985.
Financial Support:
MRC, Canada; British Columbia Lung Association.

0102. THOUGHT TECHNOLOGY LTD., 2180 Belgrave Avenue, Montreal, Quebec H4A 2L8, Canada.

Project Title:
Quit Smoking Through Biofeedback.

Principal Investigators:
McCann, B.; Corson, J.; Myers, H., et al.
Objective:
To investigate the use of biofeedback/deep relaxation and positive suggestion to enhance the ability to stop smoking and remain abstinent.
Methods or Approach:
Purchasers of the Quit Smoking Through Biofeedback pro-

gram will be sent a questionnaire on past efforts to quit smoking and experiences with the biofeedback program.

Results to Date:
Project is in a preliminary phase.

Project Dates:
December 1984–December 1986.

Financial Support:
Thought Technology Ltd.

0103. UNITE DE RECHERCHES PULMONAIRES, Sherbrooke, Quebec J1H 5N4, Canada.

Project Title:
Development of New Markers of the Inflammatory Lung Diseases. Nuclear Medicine Applications.

Principal Investigators:
Begin, R.; Bisson, G.

Objective:
To find new markers of inflammatory lung diseases by utilization of nuclear medicine radiopharmaceuticals, and develop new and original quantification procedure applied to treatment of data.

Methods or Approach:
A new technique has been developed for treatment of gallium-67 (^{67}Ga) lung scan data. The technique was applied to inflammatory lung diseases, including chronic obstructive pulmonary disease, silicosis, asbestosis, and sarcoidosis. During the evaluation process, a group of normal subjects was also studied.

Results to Date:
Concerning the problem of smoking, it was found that the ^{67}Ga index was slightly higher in smokers than in nonsmokers. In normal subjects above age 40, there was no significant difference between smokers and nonsmokers in ^{67}Ga lung uptake index, but in those below age 40, the index was significantly higher in smokers than in nonsmokers ($p<0.01$). The method can clearly differentiate subjects with mild chronic inflammation (cigarette smokers and COPD patients) from patients with well established interstitial lung diseases. The method could be of interest in serial assessment of disease activity in interstitial lung diseases and in early detection of environmental lung diseases.

Project Dates:
1980–1984.

Financial Support:
Unite de Recherche Pulmonaire, Quebec.

Reference:
Bisson, G.; Drapeau, G.; Lamoureux, G., et al. "Computer-Based Quantitative Analysis of Gallium-67 Uptake in Normal and Diseased Lungs." Chest 84(5):513-517, November 1983.

0104. UNIVERSITE LAVAL, FACULTE DE MEDECINE, Quebec G1K 7P4, Canada.

Project Title:
The CIG-ARRETE Method.

Principal Investigator:
Talbot, R.W.

Objective:
To develop a scientific method (CIG-ARRETE) designed to help people to stop smoking.

Methods or Approach:
The program is spread out over a 20-day period during which the smoker prepares mentally and physically to stop smoking. It is compiled in a book entitled "Stop Smoking for Good in 20 Days," which has specific directions to follow each day that are designed to help the smoker reach complete abstinence on the 21st day. Smokers may choose to participate in two therapy sessions (2.5 hours each, on the first and 21st days), which consist of film and slide presentations, biochemical demonstrations, and animation. In general, sessions are given in hospitals on weeknights or Saturday mornings. A nutritionally enhanced, nonmedicated lozenge is also available that satisfies the smoker's habit of putting an object in the mouth and alleviates the feeling caused by the absence of an available pack of cigarettes (lozenges are provided in a pack similar to a king-size pack of cigarettes). The lozenge takes about the same amount of time to melt as a cigarette takes to smoke. Ex-smokers may also take advantage of a smoker's telephone hot line program. A letter of congratulation and encouragement is sent a few days after a person starts the program, and a certificate is available after 3 months of abstinence. The original French version has been translated and an English program is now available.

Results to Date:
Results are not available.

Reference:
Talbot, R.W. "En 20 Jours Cessez de Fumer Pour Toujours!" Quebec, Canada, Les Livres Utilis Inc., 1984, 126 pp.

0105. UNIVERSITY HOSPITAL, Department of Medicine, Section of Respiratory Medicine, Saskatoon, Saskatchewan S7N 0X0, Canada.

Project Title:
Humboldt Lung Study of Chronic Obstructive Pulmonary Disease.

Principal Investigators:
Dosman, J.A.; Cotton, D.J.; Cockcroft, D.W., et al.

Objective:
To test the hypotheses that individuals with peripheral airways obstruction will develop loss of lung function (measured by forced expiratory flow rates) over a 6-year period, in excess of that experienced by those without evidence of such obstruction.

Methods or Approach:
In the town of Humboldt, 92.6 percent of the population (1,174 persons) was studied with spirometry and the single breath nitrogen test in 1977. A followup study was carried out 6 years later to test the hypothesis.

Results to Date:
Results indicated that females are more likely to develop lung dysfunction than males when matched for smoking and age.

Future Plans:
An additional 9-year followup will be conducted.

Project Dates:
June 1977–1989.

Financial Support:
Saskatchewan Lung Association.

0106. UNIVERSITY OF ALBERTA, FACULTY OF MEDICINE, 13-103 Clinical Sciences Building, Edmonton, Alberta T6G 2G3, Canada.

Project Title:
Implications of Clove Cigarette Use by Adolescent Smokers.

Principal Investigators:
Guidotti, T.L.; Schechter, F.G.

Objective:
To (1) characterize use of imported Indonesian clove-containing cigarettes (kreteks) among adolescents in California; (2) identify acute health effects related to use of kreteks by

studying two cases (one fatal) of respiratory failure in adolescents with respiratory tract infections who sustained acute decompensation after intercurrent use of kreteks; (3) identify potential chronic health effects associated with kretek use; and (4) recognize implications for conditioning of smoking behavior by initial adolescent experimentation with a nonaversive cigarette.

Methods or Approach:

Methods keyed to objectives are (1) consumption data and historical reconstruction; (2) analysis of two 1984 index cases suspected of experiencing acute health effects (possibly a "compromised host" phenomenon); (3) inhalation toxicology studies being considered; and (4) behavioral medicine analysis.

Results to Date:

The fad of smoking kretek cigarettes appears to have begun about 1980 among Southern California surfers. By 1982, it had spread throughout the world, including Canada. Suspected acute health effects have been reported to the U.S. Centers for Disease Control and Canada Laboratory for Disease Control. Active ingredient in kreteks is eugenol, a topical anesthetic and cyclooxygenase inhibitor. The likely products of combustion have not been characterized. Kreteks suppress cough and ablate aversive response to initial cigarette smoking experience, and produce pleasant mild euphoria, which may condition adolescents to early acceptance of smoking and encourage deeper inspiration of cigarette smoke.

Project Dates:

June 1982–continuing

0107. UNIVERSITY OF BRITISH COLUMBIA, VANCOUVER GENERAL HOSPITAL, Respiratory Division, Vancouver, British Columbia V5Z 1M9, Canada.

Project Title:

In-Vitro Neutrophil Elastase Release in Relation to Smoking and Airway Obstruction.

Principal Investigator:

Abboud, R.T.

Objective:

To determine the relationship between in vitro elastase release from neutrophils, following phagocytosis or chemotactic stimulation, and smoking and abnormal lung function in human subjects.

Methods or Approach:

Neutrophils were isolated in purified suspensions from 54 male subjects (24 nonsmokers and 30 smokers). Neutrophils were stimulated in vitro by phagocytosis of zymosan particles, or chemotactic stimulation by the synthetic polypeptide, formylmethionyl-leucyl-phenyl-alanine (FMLP). Release of the lysosomal enzymes, beta-glucosaminidase and elastase, was determined on the cell-free supernatants.

Results to Date:

Of the 30 smokers studied, 17 had normal lung function and 13 had abnormal lung function. Release of the lysosomal enzymes, beta-glucosaminidase and elastase, was not significantly different among nonsmokers, smokers with normal lung function, and smokers with abnormal lung function, whether release was induced by zymosan phagocytosis, or stimulation by the various concentrations of FMLP used.

Project Dates:

June 1979–July 1981.

Financial Support:

British Columbia Health Care Research Foundation.

Reference:

Abboud, R.T.; Johnson, A.J.; Richter, A.M., et al. "Comparison of *In Vitro* Neutrophil Elastase Release in Nonsmokers and Smokers." *American Review of Respiratory Disease* 128:507-510, 1983.

0108. UNIVERSITY OF BRITISH COLUMBIA, PULMONARY RESEARCH LABORATORY, St. Paul's Hospital, 1081 Burrard Street, Vancouver, British Columbia V6Z 1Y6, Canada.

Project Title:

The Effect of Cigarette Smoke-Induced Airway Inflammation on Bronchial Hyperreactivity.

Principal Investigators:

Hogg, J.C.; Walker, D.C.; Van Oostdam, J.

Objective:

To determine the mechanism by which cigarette smoke-induced airways inflammation induces bronchial hyperreactivity.

Methods or Approach:

Airways inflammation is induced with cigarette smoke in guinea pigs and airways reactivity is measured, using a recently developed technique, to investigate whether increased airways reactivity occurs during the exudative phase of the inflammatory reaction where there is mediator release or during a later phase when the polymorphonuclear cells migrate into the inflammatory reaction.

Results to Date:

Findings to date show that increased reactivity is not associated with polymorphonuclear leukocyte migration into the inflammatory reaction.

Project Dates:

April 1980–April 1986.

Financial Support:

MRC, Canada; British Columbia Lung Association.

0109. UNIVERSITY OF BRITISH COLUMBIA, Department of Psychology, Vancouver, British Columbia V6T 1W5, Canada.

Project Title:

Restricted Environmental Stimulation Therapy in Smoking Cessation.

Principal Investigator:

Suedfeld, P.

Objective:

To investigate effectiveness of restricted environmental stimulation therapy (REST) in smoking cessation.

Methods or Approach:

Other phases of the project have investigated parametric factors, combinations of REST with other behavioral modification procedures, and relative contribution of specific and nonspecific components. This phase will concentrate on prevention of smoking relapse among clients who have already quit (through REST treatment, some other intervention, or by themselves). Other behaviors related to cardiovascular problems will also be investigated. REST (usually consisting of 24 hours lying on a bed in a dark, silent chamber) is combined with periodic presentation of messages related to smoking cessation, such as stress management, coping with relapse, and predictable emotional effects of quitting. More standard behavioral treatments, including self-monitoring, satiation smoking, and covert aversive conditioning, are sometimes combined with the REST technique. Followup is conducted for at least 1 year after treatment.

Results to Date:

Long-term abstinence rates of up to 50 percent and mean reduction from baseline of over 50 percent have been found.

Exact figures vary with specific combination of procedures used. Good results have been obtained even with highly addicted smokers. The strength of the procedures appears to be in the possibility of achieving long-term maintenance (lower relapse rates) although initial success rates are usually about the same as found with other treatment procedures. Recent results indicate that a combination of 24 hours of REST with messages interspersed throughout that period is optimal. Client expectancy plays a negligible role in outcome.

Future Plans:

The next phase will concentrate on reducing relapse to a minimum with clients who have already quit but have either relapsed or feel that they are in danger of doing so. The use of flotation REST will also be explored.

Project Dates:

July 1970–continuing.

Financial Support:

NHLBI (5R01HL25918).

0110. UNIVERSITY OF BRITISH COLUMBIA, VANCOUVER GENERAL HOSPITAL, Respiratory Division, 2775 Heather Street, Vancouver, British Columbia V5Z 3J5, Canada.

Project Title:

Effect of Smoking on Plasma Trypsin and Elastase Inhibiting Capacity.

Principal Investigators:

Fera, T.; Abboud, R.T.; Richter, A.M., et al.

Objective:

To evaluate effect of smoking on levels of major plasma protease inhibitors and on plasma trypsin inhibiting capacity (TIC) and elastase inhibiting capacity (EIC).

Methods or Approach:

Immunologic levels of α_1-protease inhibitor (α_1PI), α_2-macroglobulin, and inter-α-trypsin inhibitor levels were compared in 29 smokers and 30 smokers aged 40±12 years. Plasma TIC and EIC levels were evaluated in both groups, and the acute effect of intense smoking on plasma TIC and EIC levels was determined and expressed as specific activity/immunologic α_1PI level.

Results to Date:

Plasma α_1PI levels were significantly higher in smokers than in nonsmokers; however, there was no significant difference in α_2-macroglobulin or inter-α-trypsin inhibitor levels. Plasma TIC and EIC were slightly, but significantly, lower in smokers compared with nonsmokers, but there was no difference in plasma TIC/EIC ratios in smokers compared with nonsmokers. After intense smoking, there was a slight decrease in both TIC and EIC (about 10 percent), but no significant change in TIC/EIC ratios. Effects of smoking can be detected by measurement of either elastase inhibition or trypsin inhibition, although the TIC/EIC ratio is not affected.

Project Dates:

January 1984–December 1984.

Financial Support:

British Columbia Lung Association.

0111. UNIVERSITY OF BRITISH COLUMBIA, VANCOUVER GENERAL HOSPITAL, Respiratory Division, 2775 Heather Street, Vancouver, British Columbia V5Z 3J5, Canada.

Project Title:

Acute Effect of Smoking on Elastase in Bronchoalveolar Lavage Fluid.

Principal Investigators:

Fera, T.; Abboud, R.T.; Richter, A.M., et al.

Objective:

To determine acute effect of smoking on elastase levels in bronchoalveolar lavage fluid.

Methods or Approach:

Bronchoalveolar lavage fluid (BAL) was obtained from 30 smokers who had twice had fiberoptic bronchoscopy; (1) before smoking (after 8 hours of abstinence from smoking), and (2) 2 minutes to 1 hour after smoking either two or four cigarettes. BAL was concentrated 100-fold and elastase activity determined, using succinyl-trialanyl-p-nitroanalide (SLAPN) as substrate. In some subjects, immunologic elastase levels in BAL were determined, using a sensitive enzyme-linked immunosorbent assay.

Results to Date:

There was elastase activity against SLAPN that was almost completely inhibited by EDTA, indicating that it was due to a metallo-protease. There was no change in SLAPN elastase activity in BAL after smoking compared with presmoking levels. In 10 subjects studied before and after smoking four cigarettes, immunologic neutrophil elastase levels in BAL increased significantly. Results indicate that acute smoking increases immunologic neutrophil elastase levels in BAL, but does not affect elastase activity against SLAPN. Findings suggest that smoking induces release of neutrophil elastase in bronchoalveolar lining.

Future Plans:

Plans are to correlate lavage immunologic elastase levels with immunologic elastase levels absent in cells recovered in lavage.

Project Dates:

September 1982–June 1985.

Financial Support:

MRC, Canada (MA 6892); British Columbia Health Care Research Foundation; British Columbia Lung Association.

0112. UNIVERSITY OF BRITISH COLUMBIA, VANCOUVER GENERAL HOSPITAL, Respiratory Division, 2775 Heather Street, Vancouver, British Columbia V5Z 3J5, Canada.

Project Title:

Acute Effect of Smoking on Superoxide Production by Pulmonary Alveolar Macrophages.

Principal Investigators:

Richter, A.M.; Abboud, R.T.; Johal, S.S., et al.

Objective:

To determine effects of smoking on superoxide (O_2^-) production by pulmonary alveolar macrophages (PAM).

Methods or Approach:

O_2^- production by PAM, recovered by bronchoalveolar lavage from 8 nonsmokers and 40 smokers, was determined before and after smoking either two or four cigarettes. O_2^- production was determined by reduction of ferricytochrome-C.

Results to Date:

Prior to smoking, O_2^- production was significantly greater in smokers than in nonsmokers, whether macrophages were unstimulated or stimulated by zymosan or phorbol myristate acetate. O_2^- production by unstimulated PAM increased significantly 1 hour after subjects had smoked two cigarettes, but there was no increase under other conditions. Results suggest that, in addition to the chronic effect of smoking that increases O_2^- production by PAM, there may be a stimulating effect of acute smoking. Increased O_2^- production by PAM following smoking may be a factor contributing to inactivation of alpha$_1$-protease inhibitor in bronchoalveolar lavage.

Project Dates:
June 1982–December 1984.
Financial Support:
MRC, Canada (MA-7864); British Columbia Health Care Research Foundation; British Columbia Lung Association.

0113. UNIVERSITY OF BRITISH COLUMBIA, VANCOUVER GENERAL HOSPITAL, Respiratory Division, 2775 Heather Street, Vancouver, British Columbia V5Z 3J5, Canada.

Project Title:
Effect of Smoking on Plasma Neutrophil Elastase Levels.

Principal Investigators:
Abboud, R.T.; Fera, T.; Johal, S., et al.
Objective:
To determine effect of smoking on plasma elastase, which is considered to indicate neutrophil elastase that has been released in vivo and has complexed with plasma inhibitors.
Methods or Approach:
Plasma elastase was determined with a sensitive enzyme-linked immunoassay (ELISA). Elastase levels and leukocyte and neutrophil counts were compared in healthy smokers and nonsmokers. Acute effect of smoking on neutrophil elastase levels was also determined in smokers.
Results to Date:
No significant differences in plasma elastase levels were found in smokers compared with nonsmokers, or in smokers before and after daily smoking. However, a significant increase in plasma elastase levels was found in six healthy smokers tested after 8 hours of abstinence and after smoking eight cigarettes over a 2-hour period. Neutrophil elastase levels were significantly increased 1 hour after smoking, but were not significantly different 2 hours after completion of smoking. Results suggest that intense smoking may lead to acute elevation of plasma elastase, suggesting in vivo release of elastase.
Future Plans:
An attempt will be made to correlate levels of elastase in bronchoalveolar lavage induced by intense smoking with plasma elastase levels.
Project Dates:
July 1984–December 1985.
Financial Support:
MRC, Canada (MA-6892); British Columbia Health Care Research Foundation; British Columbia Lung Association.

0114. UNIVERSITY OF BRITISH COLUMBIA, VANCOUVER GENERAL HOSPITAL, Respiratory Division, 2775 Heather Street, Vancouver, British Columbia V5Z 3J5, Canada.

Project Title:
Elastase Levels and Alpha$_1$-Antiprotease Activity in Bronchoalveolar Lavage of Upper Lobes Compared With Lower Lobes in Smokers.

Principal Investigators:
Abboud, R.T.; Richter, A.; Johal, S., et al.
Objective:
To evaluate possible factors favoring predilection for upper lobe involvement by centrilobular emphysema in smokers.
Methods or Approach:
Research compared bronchoalveolar lavage fluid from the right upper lobe with bronchoalveolar lavage fluid from the right lower lobe in volunteers (all smokers). The two lavages were performed in random sequence, about 30 minutes after smoking either four or eight cigarettes. Cell counts and differentials were determined. Cells were sedimented by centrifugation and elastase activity in alveolar macrophages was assayed using succinyl-trialanyl-p-nitroanalide as a substrate. Cell-free bronchoalveolar lavage fluid was concentrated about a hundredfold and assayed for alpha$_1$-protease level and activity, elastase activity against SLAPN, and immunologic elastase levels.
Results to Date:
Findings to date indicate no significant difference in alpha$_1$-protease levels or activity in the upper lobe compared with the lower lobe, both being fully functional. There was no difference in cell counts or differentials or elastase activity in alveolar macrophages. However, there was a significantly higher level of immunologic neutrophil elastase (expressed per µg alpha$_1$-protease inhibitor) in the upper lobe compared with the lower lobe. Findings suggest greater release of neutrophil elastase from the upper lobe following smoking, which may be a factor predisposing to more elastolytic lung injury in the upper lobe following smoking.
Project Dates:
January 1984–December 1985.
Financial Support:
MRC, Canada (MA-6892); British Columbia Health Care Research Foundation; British Columbia Lung Association.

0115. UNIVERSITY OF BRITISH COLUMBIA, VANCOUVER GENERAL HOSPITAL, Respiratory Division, Vancouver, British Columbia V5Z 1M9, Canada.

Project Title:
Acute Effect of Smoking on the Functional Activity of Alpha$_1$-Protease Inhibitor in Bronchoalveolar Lavage Fluid.

Principal Investigators:
Abboud, R.T.; Fera, T.; Richter, A., et al.
Objective:
To determine the acute effects of smoking on alpha$_1$-protease inhibitor (α_1-PI) in bronchoalveolar lavage (BAL) fluid.
Methods or Approach:
Subjects were 38 smokers (mean age 25±6.5 years) who had two fiberoptic BALs in sequence, the first after 8 hours of abstinence from smoking and the second at varying time intervals after smoking: 22 were tested before, and 10 minutes to 3 hours after smoking two medium-tar filter cigarettes; 16 were tested before and 2 minutes to 60 minutes after smoking four cigarettes. Eight nonsmoking volunteers (controls) had BAL performed in sequence.
Results to Date:
Initial BAL from controls and from smokers after 8 hours of abstinence had similar α_1-PI activity (mean 0.495±0.017 µg of pancreatic elastase/µg α_1-PI, about 90 percent of activity of purified α_1-PI). After smoking, no significant inactivation of α_1-PI was found except in the six smokers lavaged 1 hour after smoking two cigarettes, whose α_1-PI activity decreased slightly to 90.0±10.6 percent of initial activity ($p < 0.05$). BAL obtained from seven smokers only after smoking did not indicate inactivation of α_1-PI. It is concluded that in young healthy smokers (1) α_1-PI activity in BAL after 8 hours of abstinence from smoking is similar to nonsmoking controls; and (2) after smoking two to four cigarettes, there is no, or very limited, inactivation of α_1-PI.
Financial Support:
MRC, Canada (MA 6892).
Reference:
Abboud, R.T.; Fera, T.; Richter, A., et al. "Acute Effect of Smoking on the Functional Activity of Alpha$_1$-Protease Inhibi-

tor in Bronchoalveolar Lavage Fluid." *American Review of Respiratory Disease* 131:79-85, January 1985.

0116. UNIVERSITY OF BRITISH COLUMBIA, Department of Medicine, 2775 Heather Street, Vancouver, British Columbia V5Z 3J5, Canada.

Project Title:
University of British Columbia Program for Early Detection of Lung Cancer.

Principal Investigator:
Enarson, D.
Objective:
To determine whether a blood test is a reliable and economical tool for early detection of lung cancer.
Methods or Approach:
A blood test has been developed that is positive in all forms of lung cancer, negative for other cancers, and negative in healthy people without cancer. The tests are easy and inexpensive, but it not clear whether they measure the presence of only a large lung cancer or whether the test is positive at an early stage in cancer development. Management and unions at 18 mine sites in British Columbia and the Yukon agreed to cooperate in the program and all eligible persons (aged 40 years and over) will be contacted personally and invited to participate. Those who enroll will be asked to provide information on work, health, and smoking history; a sputum sample; a chest x ray; and a blood sample. About 20 percent (based on age, smoking habits, occupational history) will be seen every 6 months for a sputum test and completion of a short questionnaire on current health status. All participants will be seen within 2 to 3 years of enrollment. Letters will be sent explaining results of sputum tests and x ray. Statistical information is reported annually to participating unions and companies to show patterns of participation and symptoms at various locations; however, no individuals can be identified from this information, ensuring confidentiality.
Results to Date:
Earlier studies showed that detection by x ray and sputum tests is not economically feasible and that the tests do not detect small cell cancers.

0117. UNIVERSITY OF MANITOBA, Neonatal Neurophysiology Laboratory, 770 Bannatyne Avenue, Winnipeg, Manitoba R3E 0W3, Canada.

Project Title:
Investigation of the Effects of Maternal Use of Alcohol on the Development of the Offspring ("Fetal Alcohol Syndrome").

Principal Investigators:
Chernick, V.; Ioffe, S.V.
Objective:
To determine effects of maternal alcohol and caffeine intake and smoking on neonatal EEG, anthropometric measurements, and future psychomotor development of offspring; determine whether the degree of EEG and/or subsequent neurological and mental abnormalities are dose-dependent.
Methods or Approach:
The following groups will be studied: (1) infants of alcoholic and/or heavy drinking mothers (>2 oz of absolute alcohol/day); (2) infants of moderate drinking mothers (0.5-2 oz/day); (3) infants of mothers who drink occasionally (<0.5 oz/day); (4) infants of binge-drinking mothers; (5) infants of mothers who smoke but do not drink (<1 pack/day, <2 packs/day, or >2 packs/day); (6) infants of mothers who drink caffeine beverages but do not drink alcohol; and (7) infants of mothers who neither smoke nor drink alcohol. Offspring will be assessed at 40 and 46 weeks of gestation, and at 9, 18, 36, and 48 months of age. Measurements will include spectral density analysis of the EEG in different sleep states, anthropometric indices, and Dubowitz, Bailey and McCarthy tests.
Results to Date:
Infants of smoking mothers had lower birth weights and lengths than infants of nonsmoking mothers, but head circumference was identical. Infants of alcoholic mothers had a significantly lower birth weight, length, and head circumference than controls. Infants of smoking mothers had the same gestational age and sex ratio and Apgar score at 5 minutes as those of control mothers. The Apgar score at 1 minute was slightly but significantly lower in infants of smoking mothers. These infants also showed the same behavioral and electroencephalogram pattern.
Future Plans:
Followup will be continued to determine the long-term effects of maternal smoking, alcohol consumption, and coffee drinking through 1984. Preliminary results have been published.
Project Dates:
January 1981–1986.
Reference:
Chernick, V.; Childiaeva, R.; Ioffe, S. "Effects of Maternal Alcohol Intake and Smoking on Neonatal Electroencephalogram and Anthropometric Measurements." *American Journal of Obstetrics and Gynecology* 146(1):41-47, May 1983.

0118. UNIVERSITY OF MANITOBA, 700 Bannatyne Avenue, Winnipeg, Manitoba R3E 0W3, Canada.

Project Title:
A Randomized Trial Comparing Smoking Cessation Programs Utilizing Behavior Modification, Health Education or Hypnosis.

Principal Investigators:
Rabkin, S.W.; Kaufert, J.
Objective:
To determine efficacy of hypnosis, health education, and behavior modification programs for cigarette smoking cessation.
Methods or Approach:
A randomized clinical trial was conducted with 168 volunteers to compare the three programs. Followup data was available 3 weeks after program completion in 140 subjects. The hypnosis segment utilized the single treatment method, outlined by Speigel. The behavior modification program was based on the premise that smoking is a learned behavior in response to internal and external signals or cues. Subjects recorded smoking stimuli and were given counseling as to how to deal with those stimuli and avoid cigarette smoking. Health education was in a lecture format.
Results to Date:
There were significant reductions in reported cigarette consumption and serum thiocyanate levels in all programs compared to entry levels. However, there were no significant differences between groups with respect to proportion who quit smoking, number of cigarettes smoked, or change in serum thiocyanate. At 6-month followup, there were still no significant differences. Factors such as age, age of starting to smoke, educational level, marital status, and spouse or partner who smoked did not identify subgroups with differences in treatment outcome. Thus, hypnosis, health education, and behavior modification are equally effective programs for changing cigarette smoking.

Project Dates:
1980–1983.
Financial Support:
Manitoba Medical Services Foundation.

0119. UNIVERSITY OF MANITOBA, 700 Bannatyne Avenue, Winnipeg, Manitoba R3E 0W3, Canada.

Project Title:
Effect of Cigarette Smoking Cessation on Risk Factors for Coronary Atherosclerosis.

Principal Investigator:
Rabkin, S.W.
Objective:
To determine effect of cigarette smoking cessation on other risk factors for cardiovascular disease, specifically serum lipids, body weight, blood pressure, and blood sugar.
Methods or Approach:
Followup data was available in 140 subjects who entered a randomized trial for smoking cessation. At entry, questionnaires were administered to collect relevant data and each subject was examined for height, weight, skinfold thickness, blood pressure, blood cholesterol, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglycerides, blood sugar, and serum thiocyanate. Approximately 2 to 3 months after study entry (3 weeks after end of smoking cessation program), repeat examinations were conducted.
Results to Date:
Reported cigarette consumption fell from 28.5 to 10.6 cigarettes/day, and serum thiocyanate (biochemical indicator of extent of tobacco exposure) decreased -42.8 µmol/L. Compared with controls, decreases in consumption and serum thiocyanate were significant, as were increases in body weight and skinfold thickness. Changes in serum thiocyanate correlated significantly and adversely with changes in HDL-C, body weight, and skinfold thickness, but not with change in LDL-C, triglycerides, or blood pressure. Relationships remained significant, even after adjusting for initial measurement of variables or regression to the mean. Among those who quit smoking, HDL-C increased 5.9±1.7 mg/dL. The usual inverse relationship between body weight and HDL-C does not exist with cessation of smoking. Thus, benefits of quitting extend to favorable alterations in HDL-C, and there are no adverse effects on blood pressure, fasting blood sugar triglycerides, or LDL-C.
Project Dates:
1980–1983.
Financial Support:
Manitoba Medical Services Foundation.

0120. UNIVERSITY OF OTTAWA, Department of Family Medicine, 210 Melrose Avenue, Ottawa, Ontario K1Y 4K7, Canada.

Project Title:
Impact of Routine Advice on Smoking Cessation From Family Physicians.

Principal Investigators:
Rosser, W.W.; Stewart, P.J.
Objective:
To measure the impact of a physician giving what he/she considered appropriate advice on one visit to all smokers visiting the practice for any purpose, on 1-year followup of smoking cessation.
Methods or Approach:
After 2,000 consecutive visitors to the Ottawa Civic Hospital, Family Medicine Centre, had completed a questionnaire on their smoking status, 750 smokers were randomly allocated to one of four groups. Nonsmokers were assigned to a group receiving a green nonsmoking sticker on their chart (having no further action taken). The random allocation of the smokers included (1) a control group who completed the questionnaire at the beginning of the studies, 6 months after entry, and 12 months after entry; (2) a group who received physician advice about their smoking habits on that particular visit to the office in an attempt to motivate them to stop smoking, and also then completed questionnaires at 6 months and 1 year; (3) a group who received physician advice and had a red smoker's sticker placed on their chart in their presence by the physician on that visit; and (4) a group who received smoking cessation advice by the physician, as well as a pamphlet about why they should be motivated to stop smoking.
Results to Date:
Detailed results of the project have been published. Basically, there was no significant difference in the smoking cessation rate at 1-year followup between any of the groups. Approximately 3 percent of people were able to sustain smoking cessation during the 1 year of followup, a percentage that was similar in all four groups. It is concluded that a single episode of smoking cessation intervention by a physician on a visit for any purpose had no effect on 1-year followup smoking cessation.
Future Plans:
A trial of three different methods of smoking cessation is in progress.
Project Dates:
January 1979–March 1981.
Financial Support:
University of Ottawa.
Reference:
Stewart, P.J.; Rosser, W.W. "The Impact of Routine Advice on Smoking Cessation From Family Physicians." *Canadian Medical Association Journal* 126:1051-1054, May 1, 1982.

0121. UNIVERSITY OF OTTAWA, SCHOOL OF MEDICINE, Faculty of Health Sciences, 210 Melrose Avenue, Ottawa, Ontario K1Y 4K7, Canada.

Project Title:
Randomized Control Trial of Three Different Methods of Promoting Smoking Cessation in a Family Practice.

Principal Investigators:
McDowell, I.; Mothersgill, C.; Rosser, W.W.
Objective:
To evaluate three different methods of intervention for smokers who are recruited on a visit to their family physician for any purpose; develop practical methods to promote smoking cessation that can be utilized in family practice, both in urban and nonurban locations.
Methods or Approach:
Approximately 500 smokers have been recruited into a trial, and all have completed extensive questionnaires about their previous smoking habits, as well as an assessment of their psychological status. The smokers are then randomly allocated to (1) a control group on which no further action takes place except for a 1-year followup; (2) a physician intervention group that is visited by their physician who discusses smoking cessation, and that utilizes a program developed by the National Cancer Institute for use in a physician's office, which includes a patient assessment or evaluation questionnaire,

booklets, and brochures; (3) a self-help group lead by a health education specialist, in which people attend eight evening classes using the program known as Operation "Kick It"; and (4) a psychologist-led group using behavioral modification techniques in evening sessions. Information on intake characteristics, smoking cessation rates, and dropout rates of all participants will be recorded. Also, characteristics that might be identified by a family physician suggesting that people would do better in one of the three programs are also being obtained.

Results to Date:
Preliminary results on approximately 30 people in each of the four groups at 1-year followup are showing that there is a significant difference between the physician intervention group and the self-help intervention group and the control group.

Project Dates:
September 1981–April 1983.

Financial Support:
Ministry of Health, Canada (DM-472).

Reference:
Stewart, P. J.; Rosser, W. W. "The Impact of Routine Advice on Smoking Cessation From Family Physicians." *Canadian Medical Association Journal* 126:1051, May 1, 1982.

0122. UNIVERSITY OF OTTAWA, SCHOOL OF NURSING, 451 Smyth Road, Ottawa, Ontario K1H 8M5, Canada.

Project Title:
2001, A Breath Odyssey.

Principal Investigator:
Choi-Lao, A.T.H.

Objective:
To develop an activity book on smoking and health for children of fourth and fifth grades designed to increase children's awareness of the effects and costs of smoking; identify psychosocial factors that promote smoking in a young person.

Methods or Approach:
This activity book consists of two parts. In part I, stories told about two visitors from outer space discovering Earth and the smoking habit of its earthlings, covers anatomy, physiology, mathematics, history, geography, and language. In part II, children's work projects on smoking and health are presented. Children were invited to enter a contest in four categories: poetry, short story, comic strip, and poster. Selected winning entries have been included in the book.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Changes in knowledge, attitudes, and smoking patterns of the children exposed to this activity book will be examined.

Project Dates:
September 1981–1984.

0123. UNIVERSITY OF TORONTO, NCIC Epidemiology Unit, McMurrich Building, Toronto, Ontario M5S 1A8, Canada.

Project Title:
National Breast Screening Study.

Principal Investigators:
Miller, A.B.; Baines, C.J.; Howe, G.R., et al.

Objective:
To (1) assess place of mammography and physical examination in screening women aged 40 to 49; (2) assess any additional benefit from mammography over and above screening by physical examination in women aged 50 to 59; (3) assess risk factors as indicators for those who should be screened; and (4) study the natural history of breast cancer and cost benefit of screening.

Methods or Approach:
Women aged 40 to 59 are recruited to screening centers. After completing questionnaires and signing informed consent forms, all have initial physical examination of the breasts and are taught breast self-examination. All are randomized to either mammography or no mammography. Those aged 40 to 49 who do not receive mammography do not return to the screening center, but do remain under community care. All others return for three or four repeat annual visits.

Results to Date:
Analysis of risk factors associated with breast cancer detection (identified on first screening) suggests that in women aged 40 to 49, smoking predicts breast cancer detection and that there is a dose–response relationship. There is no clear association for women aged 50 to 59.

Future Plans:
The remaining cancers diagnosed on first examination and those diagnosed on repeat screenings will be analyzed for association of smoking and screen detection, to evaluate whether or not the association noted was causal.

Project Dates:
January 1980–March 1988.

Financial Support:
HWC, Ontario Ministry of Health; NCI Canada; Canadian Cancer Society.

0124. UNIVERSITY OF TORONTO, Department of Preventive Medicine and Biostatistics, Toronto, Ontario M5S 1A8, Canada.

Project Title:
Epidemiology of Cervical Dysplasia: A Case-Control Study.

Principal Investigators:
Clarke, E.A.; McKeown Eyssen, G.E.; Lickrish, G.M.

Objective:
To examine the relationship between cigarette smoking and cervical dysplasia (a precursor of invasive cancer of the cervix).

Methods or Approach:
The 250 newly diagnosed cases and 500 controls matched by age and neighborhood were interviewed to obtain data on date of birth, education, marital status, medical care, gynecological and obstetrical history, contraceptive practices, sexual history, and smoking habits. Biopsy material from the cervix was reviewed by a single pathologist to ensure that cases were correctly diagnosed as having mild, moderate, or severe dysplasia.

Results to Date:
Initial analysis showed an increased risk associated with a history of more than two sexual partners, first intercourse before the age of 18, current smoking, education, and use and duration of use of oral contraceptives. However, the significantly increased risk of use and duration of use of oral contraceptives and education disappeared after adjustment for indices of sexual behavior and pill use. This finding does not confirm previously reported adverse effects of pill use. The relationship between smoking and cervical dysplasia might be explained by some agent in cigarette smoke depressing the immune mechanism, thus permitting a sexually transmitted agent to result in abnormal cellular development leading to onset of cervical dysplasia.

Future Plans:
A detailed analysis of smoking habits (age group, duration of smoking, amount smoked, years since cessation) and severity of cervical dysplasia (mild, moderate, severe) will be conducted.
Project Dates:
April 1979–April 1986.
Financial Support:
Ontario Cancer Treatment and Research Foundation.

0125. UNIVERSITY OF TORONTO, MOUNT SINAI HOSPITAL, 600 University Avenue, Toronto, Ontario M5G 1X5, Canada.

Project Title:
Studies on Chronic Airflow Limitation.

Principal Investigator:
Zamel, N.
Objective:
To determine the influence of cigarette smoking on airway reactivity and its relationship to blood levels of vitamin C.
Methods or Approach:
A group of nonsmokers and smokers are being compared with regard to levels of vitamin C in the blood and airway response to inhaled methacholine. Partial flow–volume curves are used as a measure of airway response to methacholine aerosol inhalation and dose responses are obtained.
Results to Date:
Project is in a preliminary phase.
Future Plans:
Full dose response of airways to nonspecific agents in smokers and nonsmokers will be compared.
Project Dates:
July 1984–July 1986.
Financial Support:
MRC, Canada (MA 6379).

0126. UNIVERSITY OF TORONTO, GAGE RESEARCH INSTITUTE, 223 College Street, Toronto, Ontario M5T 1R4, Canada. UNIVERSITY OF TORONTO, SCHOOL OF PHYSICAL AND HEALTH EDUCATION, 320 Huron Street, Toronto, Ontario M5S 1A1, Canada.

Project Title:
Pulmonary Function Responses to "Passive Smoking" and the Influence of Suggestibility.

Principal Investigators:
Urch, B.; Shephard, R.J.; Silverman, F., et al.
Objective:
To (1) determine whether nonsmoking, nonasthmatic subjects show a physiologically important acute change of nasal airflow resistance, pulmonary function, and exercise variables in response to machine-produced cigarette smoke under a combination of high smoke concentrations and intermittent exercise sufficient to increase ventilation by a factor of 5.0; (2) test the same objective with nonsmoking, asthmatic subjects; and (3) test the hypothesis that acute changes of pulmonary function observed in a proportion of subjects who claim sensitivity to cigarette smoke are due to autosuggestion rather than pharmacological or allergic response to smoke.
Methods or Approach:
Nonasthmatic nonsmokers and asthmatic nonsmokers are exposed for 65 minutes on three separate occasions to sham, moderate (15 to 19 ppm carbon monoxide (CO)), and heavy (34 to 38 ppm CO) concentrations of cigarette smoke, in a 15 m^3 chamber. A preliminary visit is used for orientation and habituation to procedures and to measure baseline pulmonary function and assess suggestibility with standard psychological tests. During exposure, nonasthmatics perform intermittent exercise (2 sessions, 15 minutes each). Asthmatics are exposed to the same smoke concentrations but are at rest during exposure. Cigarette smoke generated by a machine (located outside the exposure chamber but visible to subjects) is directed into or away from the chamber. Measures of pulmonary function, nasal airflow resistance, ventilation, heart rate, and galvanic skin response are measured at various points during exposure. After exposure, a questionnaire of subjective reactions is administered, and tests of pulmonary function, carboxyhemoglobin rebreathe estimation, and a cycle ergometer submaximum exercise test (nonasthmatics only) are performed.
Results to Date:
Among nonasthmatics, standard respiratory test measurements showed a small decrement from sham to cigarette smoke exposure, with a large variability in response (e.g., one subject had a 26.8 percent decrease and one a 9.1 percent increase in FEF$_{50}$). There were no consistent significant differences between the two concentrations of cigarette smoke, nor were there consistent progressive changes over 60 minutes of exposure. Symptom complaints of eye irritation, odor in the exposure chamber, and throat irritation were predominant. There was a progressive increase in both the number of subjects reporting symptoms and severity of the mean symptom rating score (0 to 5 scale) from sham to moderate to heavy smoke. Other symptoms (cough, sputum, shortness of breath, nasal discharge, nasal stuffiness) showed progressive increase in mean symptom rating score from sham to moderate to heavy smoke exposure, but there was no statistically significant dose–response relationship.
Future Plans:
Analysis of suggestibility measures and pulmonary function responses during smoke exposure will be completed in nonasthmatic subjects; exposure of asthmatics will be conducted and data will be analyzed.
Project Dates:
October 1982–September 1985.
Financial Support:
HWC.

0127. UNIVERSITY OF WATERLOO, Department of Health Studies, Waterloo, Ontario N2L 3G1, Canada.

Project Title:
Smoking Prevention in the Schools: Program Dissemination.

Principal Investigators:
Best, J.A.; Brown, K.S.
Objective:
To (1) provide a clear test of efficacy of a school-based smoking prevention program among students in grades 6-8; (2) compare the relative efficacy of the program with that which is currently most often used in these grades in Ontario; (3) study the major environmental influences on smoking onset; (4) develop and evaluate training procedures suitable for a range of potential program providers; (5) test, experimentally, the relative efficacy of face-to-face provider workshop training versus printed training manuals; and (6) produce program and provider training manuals for possible dissemination.
Methods or Approach:
This program is the second phase of a project designed to develop a smoking prevention curriculum to be implemented across the province of Ontario. The program was developed

and a formative/process evaluation was completed in Phase I. Phase II includes two studies over a 4.5-year period. In Study 1, which began in January 1983, 75 matched schools with grade 6 classrooms were randomly assigned to one of five conditions. The design will provide a summative evaluation, a control for effects of repeated process evaluation, and a comparison with an existing program. The program focuses on increasing awareness of the social pressures that influence smoking onset and teaching coping skills to prevent initiation. The core program is given in grade 6 with "booster" sessions in grades 7 and 8. Students in all but the minimal testing control are intensively examined twice a year from grade 6 to grade 8. Saliva thiocyanate is collected to validate self-reported smoking behavior. In Study 2, scheduled to begin in 1986, matched schools will be assigned to one of six conditions in a complete factorial design where three types of program providers (classroom teacher, community and health volunteers, and health educators) are crossed with two types of training (workshops vs. printed manual).

Results to Date:
Results from the Phase I evaluation of the smoking prevention program show that at the end of grade 7, 18 months after treatment, the program has had a significant impact on cigarette smoking, with students in the control group experimenting with smoking at a rate 2.6 times greater than those in the treatment group. Analyses indicate that the program has been most successful for those students who had the most immediate inclinations to smoke at the beginning of grade 6.

Future Plans:
Phase III of the project will cover the province-wide dissemination and evaluation of the smoking prevention program.

Project Dates:
July 1982–1985.

Financial Support:
Ontario Ministry of HWC; Ontario Heart Foundation; HWC, Canada.

0128. UNIVERSITY OF WATERLOO, FACULTY OF MATHEMATICS, Department of Statistics, Waterloo, Ontario N2L 3G1, Canada.

Project Title:
Economic Benefits and Losses Associated With Cigarette Smoking.

Principal Investigators:
Forbes, W.F.; Thompson, M.E.

Objective:
To assess the economic benefits and losses associated with smoking in different countries.

Methods or Approach:
Data are collected from the literature, and the main benefits and costs/risks are considered. These are also considered separately, depending on whether they apply to the individual, to the family, or to society. The main benefits and costs considered with respect to society are the health care costs, the loss in productivity, the benefits of the tobacco industry, the employment of marketers and distributors, and the savings in pensions to smokers dying prematurely.

Results to Date:
Studies have been completed for Canada. Results to date indicate that there is an imbalance for countries such as Canada, and it appears that the economic losses associated with cigarette smoking are greater than the benefits.

Future Plans:
Studies will be extended to the United States, countries in which no tobacco is grown, and also to some selected developing countries. The role of taxation in affecting cigarette consumption will be investigated.

Project Dates:
1977–1985.

Financial Support:
WHO.

0129. UNIVERSITY OF WATERLOO, FACULTY OF HUMAN KINETICS AND LEISURE STUDIES, Department of Health Studies, Waterloo, Ontario N2L 3G1, Canada. MCMASTER UNIVERSITY, FACULTY OF HEALTH SCIENCES, Health Sciences Centre, 1200 Main Street West, Hamilton, Ontario L8N 3Z5, Canada.

Project Title:
Compliance With Nicotine-Bearing Chewing Gum.

Principal Investigators:
Best, J.A.; Gilbert, J.R.; Wilson, D.M.C., et al.

Objective:
To (1) evaluate the impact of procedures designed to improve patient compliance with a nicotine chewing gum (NCG) regimen compared with NCG prescription alone, with respect to initial acceptance of NCG prescription, gum compliance per se, and prevalence of smoking at 1-year followup; (2) identify factors affecting physician compliance with a recommended NCG prescription protocol; (3) develop procedures designed to improve compliance; and (4) describe the typical cessation process following NCG prescription in each experimental condition with respect to (a) frequency, regularity, and duration of NCG use and situational and/or physiological factors associated with use; (b) continuing smoking behaviors, urges, and withdrawal symptoms; and (c) factors influencing continuation or noncontinuation of NCG use, and relapse episodes.

Methods or Approach:
The project includes a randomized trial, a process evaluation component, and a formative evaluation component. The randomized clinical trial is to test the efficacy of a simple compliance-enhancing protocol to be used in prescribing NCG. The proportion of study patients smoking at 1 year in each participating practice is the primary endpoint. Ninety general or family physicians have been randomly assigned to (1) usual care, in which the doctor does not modify usual procedures with patients who smoke; (2) gum only, in which patients are advised to quit smoking and are offered a prescription for NCG; and (3) gum plus compliance enhancement, in which physicians are trained in optimal methods of NCG prescription, patients are followed according to a preset schedule that offers five return appointments, and there is a written commitment to the patient's chosen response to advice and NCG offer. Process evaluation will determine what people go through when they are trying to quit smoking. One hundred patients will be recruited through three family practice physician offices, and excluded from the main study. Fifty patients will be interviewed using ethnographic (anthropological) open-ended interviewing methods, and the remaining fifty will be studied using behavioral psychological measures to determine smoking urges, withdrawal symptoms, cessation problems, and experience. The formative evaluation component will collect information on program implementation, patient and physician compliance with the protocol, and physician–patient interactions.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Data will be used to plan future studies to further increase physician impact on smoking prevalence by increasing and improving physician use of an NCG protocol, and by complementing NCG compliance enhancement procedures with additional behavioral management techniques as necessary.
Project Dates:
October 1984–March 1987.
Financial Support:
NCI (1R01CA38334-01).

0130. UNIVERSITY OF WESTERN ONTARIO, Department of Epidemiology and Biostatistics, Kresge Building, London, Ontario N6A 5B7, Canada.

Project Title:
Smoking Cessation Among Patients Hospitalized With Pulmonary Disease.

Principal Investigators:
Pederson, L.L.; Lefcoe, N.M.
Objective:
To evaluate the effectiveness of intense smoking cessation procedures for patients hospitalized with acute exacerbation of respiratory symptoms.
Methods or Approach:
The subjects will be 74 patients with diagnosed pulmonary disease seen at Victoria Hospital, Westminster Campus, in the Pulmonary Unit. These patients would ordinarily be hospitalized for their respiratory disease (asthma, bronchitis, emphysema, and bronchiectasis). Patients will be randomly assigned to one of two groups. One group will undergo intensive smoking cessation procedures in addition to treatment for their chest conditions. These procedures will involve individual counseling and using a self-help manual. The second group will constitute a control condition and will undergo usual treatment for their chest disease but no special treatment for smoking. The proportion of successful quitters in the treated group will be compared to the proportion in the untreated controls. Telephone followup will be carried out at 1, 3, and 6 months following release from hospital to determine smoking status. During the stay in the hospital, corroboration of verbal report of smoking status will be requested from hospital staff. Serum thiocyanate analysis will be carried out at the 6-month followup to corroborate the verbal report.
Results to Date:
Followup is almost complete; analyses will be carried out and results prepared for publication.
Future Plans:
Chi-square analysis on the proportion of successful abstainers in each group will be made and multiple logistic regression analysis will be carried out to determine which patient and/or diagnostic characteristics are predictive of successful outcome in the two groups. If the proportion of successful quitters is significantly larger in the treated group, this program will be undertaken as part of routine hospital procedure for pulmonary patients.
Project Dates:
February 1981–1982.
Financial Support:
National Health Research Scholar Award; Ontario Thoracic Society.
Reference:
Pomerleau, O.F.; Pomerleau, C.S. "Break the Smoking Habit. A Behavioral Program for Giving Up Cigarettes." Champaign, Illinois, Research Press, 1977, 141 pp.

0131. UNIVERSITY OF WESTERN ONTARIO, Department of Epidemiology and Biostatistics, Kresge Building, London, Ontario N6A 5B7, Canada.

Project Title:
Six-Year Follow-Up of Cigarette Smoking Among a Cohort of Public Students.

Principal Investigators:
Pederson, L.L.; Lefcoe, N.M.
Objective:
To (1) assess developmental trends in smoking in school students first surveyed in 1975 (grades 4 through 6) and followed up in 1978 (grades 6 through 8); (2) investigate initiation to smoking; (3) examine the success of attempting to identify high-risk children at an early age; (4) gain insight into the direction of causal relationships; and (5) evaluate effects of exposure to smoking awareness material.
Methods or Approach:
All students who completed the questionnaire in 1975, 1978, or both will participate (n=3,273 students). The cohort will range in age from 14 to 18 years and be in grades 10 through 12 (if still in school). Attempts will be made to locate the total sample. The self-administered questionnaire will be a modification of the one used in previous testings and will contain items on knowledge, attitude, sociodemographic characteristics, smoking environment, and smoking behavior. Thiocyanate analysis will be carried out on a random sample of 200 respondents, to verify written reports of smoking status.
Results to Date:
Data collection has been completed and analyses are continuing. Results will be prepared for publication.
Future Plans:
Descriptive statistics will be obtained and bivariate relationships examined. Multivariate statistical analyses will be carried out in order to examine long-range prediction of smoking behavior over 3- and 6-year periods. Change in smoking status from one period to another will be determined and variables related to that change investigated. In addition, long-term effects of exposure to antismoking material will be examined.
Project Dates:
Fall 1982–1983.

0132. UNIVERSITY OF WESTERN ONTARIO, Department of Epidemiology and Biostatistics, Kresge Building, London, Ontario N6A 5B7, Canada.

Project Title:
Factors Related to Successful Smoking Cessation in General Practice Patients.

Principal Investigators:
Pederson, L.L.; Strickland, C.
Objective:
To (1) evaluate the effectiveness of family practitioners as smoking cessation counselors; (2) determine a set of variables that predict cessation of smoking; and (3) attempt to explain why some patients follow this advice and others do not.
Methods or Approach:
The subjects for this investigation will be 300 adults (between 18 and 70 years old) who are patients of family physicians in London, Ontario. All will be cigarette smokers who have been given advice to quit smoking by their physicians, even though they may have been seen for reasons not necessarily related to their smoking. The information will be collected by self-administered questionnaires. The physicians will provide information on diagnosis, intensity of quit smoking advice, and prediction of the patients' future smoking status. Patients will

provide information on sociodemographic characteristics, smoking history variables, health beliefs, preventive health measures, self-concept, locus of control, and self-esteem. Followup assessment of smoking status will be obtained 6 months after return of the first questionnaire.

Results to Date:
Project has been completed; a manuscript has been submitted for publication.

Future Plans:
Multivariate statistical analysis will be carried out in order to determine which set of variables best predicts successful cessation of smoking defined as at least 6 months of total abstinence. In addition, multivariate logistic models will be used to examine which variables could serve as possible explanatory constructs in accounting for successful abstention from cigarettes vs. continued smoking. Results of these analyses will be useful in future intervention research designed to assist patients who want to stop smoking.

Project Dates:
March 1981–1983.

Financial Support:
National Health Research Scholar Award.

0133. UNIVERSITY OF WESTERN ONTARIO, Department of Epidemiology and Biostatistics, Kresge Building, London, Ontario N6A 5B7, Canada.

Project Title:
Utility of a Logistic Model for Predicting Smoking Cessation Among Patients With Pulmonary Disease.

Principal Investigator:
Pederson, L.L.

Objective:
To determine the predictive accuracy of a multivariate logistics model developed for classifying pulmonary disease patients as to whether they would quit smoking following advice from a respiratory specialist to do so, based on the following variables: patient prediction, age, addiction as the major reason given for smoking, desire for quitting, educational level, socioeconomic status, number of children at home, and married as compared to not married.

Methods or Approach:
A study to validate this model was instituted. Two of the respiratory specialists who participated in the original study are providing referrals. Data were collected from 64 new patients (39 men and 25 women, all heavy smokers) over a 6-month period. Predictions from the original logistic model were made concerning future smoking among this group of patients, and predictions were verified by obtaining information on their actual behavior. Overall accuracy of prediction was 89.6 percent, but sensitivity of the model was low (44.4 percent) with a cutoff probability of 0.50. When the cutoff probability was lowered to 0.20, sensitivity was increased and accuracy remained high.

Results to Date:
Project has been completed and results published.

Project Dates:
November 1980–1982.

Financial Support:
National Health Research Scholar Award.

Reference:
Pederson, L.L.; Baskerville, J.C. "Multivariate Prediction of Smoking Cessation Following Physician Advice to Quit Smoking: A Validation Study." *Preventive Medicine* 12:430-436, 1983.

0134. UNIVERSITY OF WESTERN ONTARIO, Department of Psychology, London, Ontario N6A 5C2, Canada.

Project Title:
Caffeine Use and Dependence - Commonalities With Abuse of Other Substances.

Principal Investigator:
Graham, K.

Objective:
To test a general model of substance abuse by using predictors of alcohol abuse, smoking, and obesity to predict caffeine use and dependence.

Methods or Approach:
Undergraduates will be given a questionnaire containing measures of present coffee and tea consumption by self and friends, past consumption, reasons for consuming coffee and tea, early separations from parents, recent stressful life events, adolescent rebelliousness or deviance, and smoking and alcohol consumption.

Results to Date:
Data collection is in progress.

Project Dates:
1983–1985.

Financial Support:
University of Western Ontario.

0135. UNIVERSITY OF WESTERN ONTARIO, FACULTY OF PHYSICAL EDUCATION, London, Ontario N6A 3K7, Canada.

Project Title:
The Effect of a Program of Aerobic Exercise on the Smoking Behaviour of a Group of Adult Volunteers.

Principal Investigators:
Hill, J.S.; Paterson, D.; Noble, E.

Objective:
To explore the possible use of aerobic exercise as an intervention strategy in smoking cessation.

Methods or Approach:
Ninety volunteer cigarette smokers who wish to quit will be randomly assigned to one of three groups: (1) standard group counseling smoking cessation program plus an aerobic fitness program; (2) standard group counseling; and (3) control group. The two experimental groups will meet twice/week for 10 weeks. Testing will be conducted immediately before start of treatment, immediately following treatment, and at 1, 3, and 6 months following end of treatment. Data collected will include an extensive smoking history, body weight, fitness level, resting heart rate, blood serum thiocyanate level, and self-motivation inventory.

Results to Date:
Project is in a preliminary phase.

Project Dates:
May 1985–December 1985.

0136. UNIVERSITY OF WESTERN ONTARIO, UNIVERSITY HOSPITAL, P.O. Box 5339, Postal Station A, London, Ontario NG1 5A5, Canada.

Project Title:
Regional Deposition of Particles in the Lung During Cigarette Smoking.

Principal Investigators:
Pearson, M.G.; Vinitski, S.; Chamberlain, M.J., et al.

Objective:
To determine regional deposition of particles in the lung during cigarette smoking.
Methods or Approach:
Ventilation scans with a nebulizer-generated aerosol of submicron, technetium-labeled, sulfur colloid particles are well established. The method was adapted for use during smoking by means of a cigarette "holder" designed to permit inhalation of equal volumes of smoke and aerosol in a manner similar to smoking a filter-tipped cigarette. Eleven volunteers, with normal spirometric values, smoked two cigarettes using the special holder; resulting images were recorded on a computerized gamma camera aquisition system. On a separate day, a resting ventilation aerosol scan was performed followed by the smoking of their normal cigarette. Breathing patterns were monitored with inductance plethysmograph (Respitrace).
Results to Date:
All subjects had increased central deposition during smoking and also significant shift of deposition toward lung apices ($p<0.001$). Both lateral views indicated that the major shift was a lobar one toward the upper lobe, which in three subjects was such that upper lobe deposition exceeded lower lobe deposition. Respitrace analysis confirmed that the holder did not affect smoking patterns, but that, although each subject inhaled the bolus a little faster and more deeply than tidal breaths, no one parameter correlated with deposition pattern. These new observations offer a possible explanation for the apical localization of centrilobular emphysema.
Financial Support:
Ontario Thoracic Society.

0137. UNIVERSITY OF WESTERN ONTARIO, Department of Epidemiology and Biostatistics, Room K3D, Kresge Building, London, Ontario N6A 5B7, Canada.

Project Title:
The Use of Nicorette Chewing Gum and Self-Help Smoking Cessation Manuals for Patients With Chronic Obstructive Pulmonary Disease (COPD).

Principal Investigators:
Pederson, L.L.; Lefcoe, N.M.
Objective:
To (1) compare abstinence rates and smoking levels among groups receiving active Nicorette (2 and/or 4 mg) and no gum at 1, 6, and 12 months after initial visit to respiratory specialist; (2) compare abstinence rates and smoking levels between group receiving a self-help smoking cessation manual written for COPD patients and a group not receiving the manual at 1, 6, and 12 months; (3) identify best combination of Nicorette and manual usage for smoking cessation or reduction; and (4) identify patient subgroups predisposed to greater probability of abstention or reduction of smoking among nicotine gum users, self-help manual users, and among all study patients, controlling for any effect of the two intervention factors and their interaction.
Methods or Approach:
Patients will be randomly assigned to one of four groups (counterbalanced for three centers in London, Hamilton, and Toronto): Nicorette gum, self-help manual, gum and manual, or neither gum nor manual. Patients assigned to manual groups will receive either the self-help manual written for COPD patients or a minimal information manual (control). After 1 month, subjects will be contacted by phone to determine gum usage where appropriate, use of manual, side effects, and smoking status. At 6 months, patients will complete a self-administered mail questionnaire. Patients will return to the clinic at 12 months to complete another questionniare and for saliva thiocyanate and pulmonary function testing. Analyses will allow evaluation of the relative importance of the interventions, predisposing factors, and their combination in explaining observed outcomes with respect to abstinence. Multiple regression analysis or analysis of covariance will be used to compare changes in number of cigarettes smoked (quantitative rather than qualitative response). Incidence of side effects will be tabulated for each group. Thiocyanate and carboxyhemoglobin results will be used to validate reported abstinence.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–December 1986.
Financial Support:
Merrell-Dow Pharmaceuticals Inc., Toronto, Canada.

0138. UNIVERSITY OF WESTERN ONTARIO, Department of Epidemiology and Biostatistics, Room K3D, Kresge Building, London, Ontario N6A 5B7, Canada.

Project Title:
Survey of Knowledge and Attitudes Toward Smoking and Restrictive Measures Against Smoking in the Province of Quebec.

Principal Investigators:
Pederson, L.L.; Lefcoe, N.M.; Ashley, M.J.
Objective:
To (1) assess knowledge of existing smoking restrictions in the province of Ontario; (2) determine attitudes toward increasing restrictions (in relation to a variety of public places); (3) determine attitudes toward which level of government (if any) should enact and enforce legislation; (4) compare knowledge and attitudes among smokers, nonsmokers, and ex-smokers; and (5) compare knowledge, attitudes, and current levels of smoking among groups of rural and urban dwellers.
Methods or Approach:
The target population included all residents of voting age in Ontario. A three-stage stratified cluster design was employed to obtain a representative probability sample. The 100 primary sampling units (PSUs) selected as first stage were 1981 census subdivisions or parts of subdivisions. PSUs were separated into three strata: (1) census subdivisions with rural designation (18); (2) census subdivisions with urban designation and no existing by-laws restricting smoking; and (3) parts of census subdivisions with urban designation and existing by-laws restricting smoking (24). The second stage involved selection of households with active telephones from each of the 100 PSUs, accomplished by a random digit dialing procedure. In the third stage, one member of the household was randomly selected from a list of all appropriate respondents. Approximately 1,200 interviews were needed to give a 95 percent probability of detecting a majority as great as 60 percent in favor of, or opposed to, some restriction of smoking in specified locations.
Results to Date:
Data collection is complete and analyses are in progress. Results will provide information that can be considered in the enactment of legislation to restrict or prohibit smoking in the province. Since enforcement can be difficult, predicted compliance by both the whole group and by individual smokers will provide information on how effective any legislation is likely to be. Comparisons of urban areas with and without municipal by-laws with regard to attitudes, knowledge, and rates of smoking will give an indication of what the potential effects of increasing restrictions in other areas might be.

Project Dates:
April 1983–March 1985.

Financial Support:
Ontario Ministry of Health (00678).

CHILE

0139. HOSPITAL DEL SALVADOR, Departamento de Cirugia, Santiago, Casilla 70 D, Chile.

Project Title:
Deterioration of the Microcirculation in Diabetes Mellitus. Is Smoking a Risk Factor?

Principal Investigators:
Acevedo, A.; Schnell, A.; Toledo, L., et al.

Objective:
To study the effect of smoking on symptoms of microangiopathy in diabetes mellitus patients in the degerative stage of the disease.

Methods or Approach:
In hospitalized diabetic patients with wound-healing problems, age and duration of disease were determined. Finger circulation was studied with venous occlusion plethysmography, sympathetic function with cold accommodation in the hands, and histopathology of the skin in earlobe biopsies.

Results to Date:
Diabetic patients under 40 years of age with healing problems were smokers. In earlobe biopsies, more small vessel changes were found in smokers than in nonsmokers. All diabetics had augmented PAS positive substances in small vessel walls, dilatation and round cell accumulation of small veins, and an early elastosis senilis of collagen tissue. Chronic periphlebitis was also evident in smokers.

Project Dates:
1977–continuing.

Financial Support:
Universidad de Chile, Sede Oriente, Hospital Del Salvador.

0140. SERVICIO DE SALUD METROPOLITANO ORIENTE, HOSPITAL DEL SALVADOR, Departamento de Cirugia, Santiago, Casilla 70 D, Chile.

Project Title:
Comparative Study of Microcirculation Between Smoking and Nonsmoking Diabetics.

Principal Investigators:
Acevedo, A.; Schnell, A.; Toledo, L.

Objective:
To assess the danger of smoking for diabetics.

Methods or Approach:
Research includes plethysmographic measurements of the fingers of diabetics, plethysmographic measurements of the calf and forefoot of patients with healing problems, and ultrasound Doppler measurements of leg pressures. Each patient will undergo an earlobe biopsy.

Results to Date:
Measurements show that smokers have poorer microcirculation than nonsmokers with comparable diabetic conditions. Histopathology also appears to differ between smoking and nonsmoking diabetics.

Future Plans:
The study will be expanded to include more patients.

Project Dates:
January 1980–1982.

Financial Support:
Universidad de Chile Facultad de Medicina.

0141. UNIVERSITY OF CHILE, HOSPITAL DEL SALVADOR, Departamento de Cirugia, Santiago, Casilla 70 D, Chile.

Project Title:
Effect of Cigarette Smoking on the Glycemia, Triglycerides and Fatty Acids in Healthy and Diabetic Smokers.

Principal Investigators:
Acevedo, A.; Zavala, C.; Alcayaga, M.P.

Objective:
To study the phenomenon of nicotine-provoked hyperglycemia in healthy smokers and diabetic patients; measure vasomotor reaction in the finger while smoking and during cold application.

Methods or Approach:
Smoking effect will be studied in 10 healthy controls (between 50 and 65 years of age) and 10 type II diabetics (habitual smokers with neurotrophic ulcers of the foot). Measurements of electrocardiogram, finger blood flow, and arterial blood pressure are recorded. Venous blood tests are taken 15 and 30 minutes after smoking two cigarettes (inhaling the smoke) in less than 15 minutes.

Results to Date:
Project is in a preliminary phase.

Project Dates:
March 1985 (starting date).

Financial Support:
Alexander von Humboldt Foundation, Federal Republic of Germany.

0142. SHANGHAI CANCER INSTITUTE, 270 Dong An Road, Shanghai, People's Republic of China.

Project Title:
Population-based Case–Control Study of Lung Cancer in Shanghai.

Principal Investigators:
Gao, Y.-T.; Blot, W.J.
Objective:
To establish factors associated with high risk of lung cancer among both sexes in urban area of Shanghai; determine the relative risks of smoking for cancers of different histological types in both sexes.
Methods or Approach:
Information on all new cases of lung cancer in males aged 35 to 64 and females aged 35 to 69 years between February 1984 and February 1985 is collected and patients are interviewed. The total number of cases is expected to be approximately 1,500. Controls are selected from the total population by random sampling (frequency matching). Relative risks of smoking for all types of lung cancer and for different histological types will be estimated. The contribution of smoking to lung cancer (population attributable risk of smoking for lung cancer) will also be determined. Relative risk of passive smoking by relatives in the home and persons working with smokers will be estimated.
Results to Date:
Preliminary results show that there is a strong association between smoking and squamous cell carcinoma of the lung among both males and females (RR 12.0 and 7.0, respectively). The association between smoking and adenocarcinoma is weak (RR 1.8 and 1.1, respectively). Population attributable risk of smoking among males and females over 40 years of age is estimated to be 80.5 percent and 19.3 percent, respectively. A dose–response relationship was found between cigarette consumption and serum thiocyanate, indicating that serum thiocyanate is a marker of smoking on a group comparison basis, but not on an individual basis.
Future Plans:
Since the causes of a large proportion of female lung cancer cases have not been determined, efforts will be made to determine risk factors, especially for adenocarcinoma, including possible risks associated with passive smoking.
Project Dates:
October 1983–September 1986.
Financial Support:
NCI (N01CP21012).

0143. SHANGHAI CANCER INSTITUTE, 270 Dong An Road, Shanghai, People's Republic of China.

Project Title:
Cohort Study on the Association of Smoking With Cancer and Other Diseases.

Principal Investigators:
Gao, Y.-T.; Deng, J.
Objective:
To determine the role of smoking, air pollution, and the combination of the two factors in etiology of lung cancer and other diseases.
Methods or Approach:
A cross-sectional survey of smoking habits was carried out among 220,000 persons (over 20 years of age) residing in areas of Shanghai with different levels of general air pollution. Subjects have been grouped according to smoking habits and will be followed for 5 years. Causes of death (mainly in persons over 40 years of age) will be ascertained and analyzed to establish the association of smoking with cancer and other diseases. Other factors (including diet and occupation) will also be considered.
Results to Date:
Cohorts have been followed for more than 2 years.
Project Dates:
July 1982–December 1987.
Financial Support:
National Scientific and Technical Committee of the People's Republic of China.

0144. SHANGHAI FIRST MEDICAL COLLEGE, SCHOOL OF PUBLIC HEALTH, 138 Yi Xue Yuan Road, Shanghai 200032, People's Republic of China.

Project Title:
Household Interview Survey in Urban and Rural Areas.

Principal Investigators:
Yuan, G.X.; Hua, L.S.; Long, G.Y.
Objective:
To determine health status, use of health services, health needs, health resources, and lifestyles in urban and rural areas.
Methods or Approach:
A sampling method, designed for household surveys, will be used to gather information from 25,000 households (80,000 persons). The sample will be used to make estimates for the whole country. Smoking will be one of the items in the survey.
Results to Date:
Project is in a preliminary phase.
Future Plans:
Survey data will be compared with data from developed and developing countries.
Project Dates:
February 1985–December 1986.
Financial Support:
Ministry of Public Health, People's Republic of China.

0145. SHANGHAI FIRST MEDICAL COLLEGE, SCHOOL OF PUBLIC HEALTH, 138 Yi Xue Yuan Road, Shanghai 200032, People's Republic of China.

Project Title:
Health Risk Factors Appraisal in Rural and Urban Areas in Shanghai.

Principal Investigators:
Long, G.Y.; Hua, L.S.; Hao, X.
Objective:
To determine effects of smoking, alcohol consumption, hypertension, nutrition, exercise, and stress on health and life expectancy; compare differences between rural and urban residents.
Methods or Approach:
The project will (1) determine major causes of death in Shanghai; (2) design a questionnaire to use for health risk appraisal; (3) determine risk factor distribution according to age and sex; and (4) design computer program to use in individual health consultations. A survey will be conducted in urban and rural areas.

Results to Date:
Smoking is the most harmful factor in rural areas; hypertension is the most harmful in urban areas. Risk factor prevalence is higher in males than in females.
Project Dates:
February 1984–July 1985.
Financial Support:
Ministry of Public Health, People's Republic of China.

0146. SHANGHAI INSTITUTE OF CARDIOVASCULAR DISEASES, Shanghai 200032, People's Republic of China.

Project Title:
Relation Between Cigarette Smoking and Epidemiology of Hypertension.

Principal Investigators:
Chen, H.Z.; Pan, X.W.; Guo, G., et al.
Objective:
To determine if cigarette smoking influences the prevalence of hypertension among Chinese people in rural areas.
Methods or Approach:
A mass survey on hypertension and cigarette smoking habits was conducted among inhabitants in rural Shanghai.
Results to Date:
In the survey population of 39,048 persons, frequency of cigarette smoking was 37.47 percent in males and 0.49 percent in females. Hypertension prevalence rate among smokers was 3.94 percent; among nonsmokers the rate was 4.90 percent.
Future Plans:
Studies on the relationship between hypertension and cigarette smoking habits are continuing among people in urban Shanghai.
Project Dates:
October 1982–December 1985.
Financial Support:
Shanghai Institute of Cardiovascular Diseases.

0147. SHANGHAI INSTITUTE OF CARDIOVASCULAR DISEASES, Shanghai 200032, People's Republic of China.

Project Title:
Cigarette Smoking as a Risk Factor for Myocardial Infarction.

Principal Investigators:
Chen, H.Z.; Pan, X.W.; Li, W.X.
Objective:
To determine whether cigarette smoking is an important risk factor for myocardial infarction among Chinese people.
Methods or Approach:
Consecutive cases of myocardial infarction were selected as index cases in the case–control study of risk factors for coronary heart disease.
Results to Date:
Cigarette smoking showed a greater association in myocardial infarction cases than in controls; relative risk 3.6 for the first 200 cases.
Project Dates:
January 1979–December 1985.
Financial Support:
Shanghai Institute of Cardiovascular Diseases.

0148. TIANJIN MEDICAL COLLEGE, Department of Public Health, Tianjin, People's Republic of China.

Project Title:
Smokers in a Factory in Tianjin, China.

Principal Investigator:
Wang, R.
Objective:
To (1) investigate the prevalence of smoking in a factory in Tianjun; (2) determine distribution of smoking; (3) elicit opinions about smoking among current smokers; and (4) establish effect of an antismoking program.
Methods or Approach:
In the cross-sectional study, a self-administered questionnaire was completed by current smokers in the factory. An antismoking program is being carried out to advise current smokers to quit or reduce daily consumption.
Results to Date:
Results are not yet available.
Project Dates:
November 1984–December 1985.
Financial Support:
Health Campaign Fund, People's Republic of China.

0149. TIANJIN MEDICAL COLLEGE, Department of Epidemiology, Tianjin, People's Republic of China.

Project Title:
Smokers in Medical Services in an Area of Tianjin, China.

Principal Investigator:
Wang, R.
Objective:
To elucidate opinions or feelings about smoking among current smokers who are employed in medical services in the Tianjin area.
Methods or Approach:
A self-administered questionnaire format was used to collect opinions and feelings about smoking from current smokers.
Results to Date:
Most current smokers working in medical services believe that smoking has some kind of harmful effect; however, they also claim a number of benefits from smoking. Data shows that the effect of smoking seems to be mainly psychological; most current smokers use smoking as a psychological tool rather than being simply addicted.
Project Dates:
May 1984–February 1985.
Financial Support:
Tianjin Medical College, People's Republic of China.

COLOMBIA

0150. UNIVERSIDAD DE CARTAGENA, Facultad de Odontologia, Cartagena, Colombia.

Project Title:
Cancer and Precancer of Oral Cavity in Reverse Smokers in Bolivar, Colombia.

Principal Investigator:
Quintero Gonzalez, J.

Objective:
To determine smoking habits (especially reverse smoking) in the region; determine the most frequent lesions in relationship to smoking habits.

Methods or Approach:
Patients (over 15 years of age) in three towns in the Bolivar section on the Atlantic coast of Columbia (Arjona, Carmen de Bolivar, and San Juan) were examined. The 859 cases (342 males, 517 females) were visited at home or were seen by appointment at a health center; clinical and sometimes cytological examinations were performed. Biopsies were taken from patients seen at the Odontology Faculty and the University Hospital of Cartagena. Participating personnel included medical staff (oral pathology, odontology), cytology technicians, social workers, physicians, and students. Variables studied were age, sex, site, habits, normal smoking, and reverse smoking.

Results to Date:
Among males, 298 of the 342 were smokers (32 reverse smokers); among females, 418 of the 517 were smokers (193 reverse smokers). Duration of smoking varied from 2 years to over 60 years. Cigarettes were smoked by 167 males and 224 females and calilla by 11 males and 141 females. Lesions found included palatine keratosis (among reverse smokers), 6 males and 131 females; leukoplasia, 42 males, 54 females; nicotinic palatine leukokeratosis, 22 males, 62 females; squamous cell carcinoma, 16 males, 11 females; and leukoedema, 40 males and 80 females.

Project Dates:
June 1978–January 1979.

Financial Support:
Universidad de Cartagena.

CZECHOSLOVAKIA

0151. CHARLES UNIVERSITY, Department of Medical Microbiology and Immunology, Studnickova 7, 128 06 Prague 2, Czechoslovakia.

Project Title:
Role of Tobacco Mosaic Virus in the Pathology of Disease in Humans.

Principal Investigators:
Chyle, M.; Chyle, P.

Objective:
To (1) define the role of tobacco mosaic virus (TMV) in development of neoplasia in smokers; (2) determine whether the role is direct or indirect by induction of carcinogens and/or cocarcinogens in the infected plant; (3) determine influence of various components present in tobacco on immune response; and (4) determine new standards that could be instrumental in development of safer tobacco products.

Methods or Approach:
Tobacco and tobacco products are assayed for presence of TMV by plant infectivity tests and/or by electron microscopy. The chemical composition of tobacco (especially polyphenol content) is investigated. The interaction of cells and TMV or its RNA is studied and experiments with carcinogens, cocarcinogens, and viruses are conducted. Therapeutic approaches in neoplasia are also investigated.

Results to Date:
Most tobacco products contain TMV. Natural fermentation procedures render cigar tobacco and most pipe tobaccos low in virus and polyphenol content. Viable TMV is inhaled via smoke drawn from cigarettes. Nonsmokers also acquire TMV by breathing virus-containing smoke exhaled by smokers. Formation of TMV-like particles, observed in cultures of Chinese hamster fibroblast cells inoculated with TMV-RNA, were also found in the sputum of smokers. The incorporation of tritiated uridine was doubled in human embryo cell cultures inoculated with TMV-RNA. Inoculation of TMV into cultures of the flagellate *Trichomonas vaginalis* caused changes in the enzymatic activity of the microorganism. Analysis of cells from these cultures revealed the presence of additional antigens.

Project Dates:
1971–continuing.

0152. DERER'S HOSPITAL, POSTGRADUATE MEDICAL SCHOOL, Department of Physical Medicine and Rehabilitation, Limbova 5, 833 05 Bratislava, Kramare, Czechoslovakia.

Project Title:
Psychosocial Aspects of Rehabilitation in Patients With Myocardial Infarction.

Principal Investigator:
Palat, M.

Objective:
To examine patients following myocardial infarct to assess psychosocial factors, including smoking, that are important for structuring rehabilitation programs.

Methods or Approach:
Psychological methods are used and a semantic differential is employed in the examination. Smoking is examined as a possible risk factor for myocardial infarction.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Based on results with myocardial infarct patients, the program may be used in a broad rehabilitation practice.

Project Dates:
January 1984–December 1987.

Financial Support:
Derer's Hospital, Czechoslovakia.

0153. DISTRICT INSTITUTE OF NATIONAL HEALTH, CHEST CLINIC, Hornicke 209, 284 30 Kutna Hora, Czechoslovakia.

Project Title:
Effect of Smoking on Sickness Absence Due to Respiratory Diseases in Wage-Earners.

Principal Investigator:
Kozak, J.T.

Objective:
To (1) ascertain differences in frequency and duration of certified sickness absence in smokers and nonsmokers; (2) determine costs and benefits of differences in nonsmokers; and (3) obtain economic data and arguments for antismoking programs.

Methods or Approach:
A questionnaire was developed to identify prevalence of cigarette smoking and of respiratory symptoms among 658 plant employees. Nonsmokers, ex-smokers, occasional smokers, and current smokers were identified. Certified sickness absence according to type of illness (recorded monthly and evaluated annually) is being followed longitudinally. On randomly selected days in 1982, frequency of doctor's visits by smokers and nonsmokers was recorded.

Results to Date:
Preliminary results (1981 through 1983) show mean duration of sickness absence due to respiratory diseases was significantly longer in male smokers (of more than 50 thousand cigarettes) than in nonsmokers ($p < 0.05$). In women, mean duration of absence was significantly longer in nonsmokers than in smokers ($p < 0.001$). Male smokers were 1.23 times more frequently disabled by respiratory diseases than male nonsmokers; women smokers were 1.68 times more frequently disabled by respiratory diseases than nonsmokers. In duration of absences, there was a 5 day difference between smokers and nonsmokers in sickness absence per employee per year, which represents loss of crude mean productivity of 12,400 CS crowns/year/smoker. Male smokers visited a physician 1.42 times and female smokers 1.47 times more frequently than nonsmokers.

Project Dates:
January 1981–December 1984.

Financial Support:
District Institute of National Health, Czechoslovakia.

0154. INSTITUTE FOR CLINICAL AND EXPERIMENTAL MEDICINE, Research Department of Preventive Cardiology, Videnska 800, Prague 4, Czechoslovakia 146 22.

Project Title:
Multifactorial Primary Prevention Study of Myocardial Infarction and Stroke.

Principal Investigators:
Pistulkova, H.; Widimsky, J.; Hurych, J., et al.

Objective:
To develop optimal methods of intervention for high-risk middle-aged males within the framework of primary prevention of ischemic heart disease (antismoking propaganda and diet intervention).

Methods or Approach:
Among the 5,395 males studied, 1,748 (35 percent) smoked ≥ 15 cigarettes/day. A random sample of 151 was selected and divided into three groups to determine whether smoking habits could be influenced. The first group used the "Inhala," a plastic cigarette with a filter filled with silicic acid gel impregnated with an aromatic resinoid substance such as anise, juniper, fennel, or peppermint. Volatilizing temperature of the resins is between 16° and 30° C. The second group of 20 men received psychotherapeutic treatment, participating in free discussions; the third was a control group that received no intervention.

Results to Date:
After 1 year, 24 percent, 11.8 percent, and 12 percent in groups 1, 2, and 3, respectively, were abstinent. The difference between groups 1 and 2 and between groups 1 and 3 were significant. Baseline average number of cigarettes smoked/day was 21.6, 22.5, and 23.8 for groups 1, 2, and 3, respectively; at 1 year, consumption had dropped to 11.8, 17.9, and 18.7 cigarettes/day, respectively. The difference between groups 1 and 3 is significant ($p < 0.001$).

Future Plans:
An antismoking program will be implemented following project evaluation in projects concerned with prevention and control of cardiovascular disease in the population.

Project Dates:
1977–June 1984.

Financial Support:
Institute for Clinical and Experimental Medicine, Prague.

Reference:
Pistulkova, H.; Widimsky, J.; Hurych, J., et al. "Influence of Smoking in Middle-Aged Men." *Pracovni Lekarstvi (Prague)* 23:63, 1983.

0155. KOMENSKY UNIVERSITY, Third Medical Clinic, 833 05 Bratislava-Kramare, Czechoslavakia.

Project Title:
Effect of Smoking on the Metabolic Processes of Heart Muscle.

Principal Investigators:
Gvozdjak, J.; Gvozdjakova, A.; Kucharska, J., et al.

Objective:
To study effect of cigarette smoke inhalation on oxidative and phosphorylative processes of rabbit myocardial mitochondria.

Methods or Approach:
Effects were studied in three experimental models: (1) after a single 30-minute inhalation; (2) after 2 weeks of smoking twice/day; and (3) after 8 weeks of smoking twice/day.

Results to Date:
Long-term cigarette smoking causes significant metabolic and morphological alterations to the heart muscle that can be characterized as smoke cardiomyopathy. Significant decreases in respiration and phosphorylation rates of mitochondria were found, but the respiratory control index and coefficient of phosphorylation remained unchanged. Both carbon monoxide and nicotine participate in metabolic injury.

Project Dates:
1983–1990.

Financial Support:
Czechoslovakian State Government.

Reference:
Gvozdjakova, A.; Bada, V.; Sany, L., et al. "Smoke Cardiomyopathy: Disturbance of Oxidative Processes in Myocardial Mitochondria." *Cardiovascular Research* 18:229-232, 1984.

0156. AALBORG REGIONAL HOSPITAL, Departments of Medicine, Obstetrics and Gynecology, and Clinical Chemistry, Aalborg, Denmark.

Project Title:
Effect of Smoking on Red Cell Oxygen Transport and Release in Diabetic Pregnancy.

Principal Investigators:
Madsen, H.; Ditzel, J.
Objective:
To investigate effect of smoking on red cell oxygen transport and release in pregnant diabetic women.
Methods or Approach:
Subjects were pregnant diabetics (23 smokers and 23 nonsmokers) in the third trimester. The groups were comparable with regard to blood glucose regulation (median concentration of blood glucose and glycosylated hemoglobin (Hb A_{1c}) did not differ).
Results to Date:
Red cell 2,3-diphosphoglycerate (2,3-DPG) levels were significantly lower in smokers than in nonsmokers (16.5 vs. 17.8 µmol/g Hb, $p<0.01$). P_{50} (partial pressure of O_2 at 50 percent saturation) of the oxyhemoglobin dissociation curve at actual pH and at pH 7.40 was also significantly lower in smokers (25.9 vs. 26.9 mm Hg, $p<0.01$, and 26.5 vs. 27.8 mm Hg, $p<0.01$, respectively). Red cell 2,3-DPG was significantly correlated with P_{50} at pH 7.40 ($r=0.73$, $p<0.001$). Arterial oxygen saturation was reduced to the same degree in smokers and in nonsmokers compared with healthy nonsmoking pregnant women, and no adaptive increase in hemoglobin concentration occurred in pregnant diabetic smokers. Results suggest that smoking in pregnant diabetic women impairs the adaptive increase in 2,3-DPG associated with diabetes-induced hypoxia.
Reference:
Madsen, H.; Ditzel, J. "Effect of Smoking on Red Cell Oxygen Transport and Release in Diabetic Pregnancy." *Acta Obstetricia et Gynecologica Scandinavica* 63:77-80, 1984.

0157. FIBIGER INSTITUTE, LABORATORY OF ENVIRONMENTAL CARCINOGENESIS, 70 Ndr. Frihavnsgade, DK 2100 Copenhagen, Denmark.

Project Title:
Effect of Tobacco Smoke Components on the Expression of Different Keratins In Vitro.

Principal Investigators:
Autrup, H.; Christensen, J.L.
Objective:
To investigate effect of tobacco smoke condensate and its components on expression of keratins in cultured human buccal mucosa cells.
Methods or Approach:
The toxicity of cigarette smoke condensate on human buccal mucosa will be established by colony-forming efficiency and population doubling/day. Effects of long-term treatment of mucosa cells with a nontoxic dose of cigarette smoke condensate on keratin expression will be investigated by electrophoretic and immunological methods.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–December 1986.

Financial Support:
Neye Foundation.

0158. FIBIGER INSTITUTE, LABORATORY OF ENVIRONMENTAL CARCINOGENESIS, Department of Oral Pathology, Royal Dental School, Aarhus, Ndr. Frihavnsgade 70, DK 2100 Copenhagen O, Denmark.

Project Title:
Metabolism of Tobacco Carcinogens by Human and Rat Oral Mucosa Cells.

Principal Investigators:
Autrup, H.; Jepsen, A.; Dragsted, L.
Objective:
To investigate metabolic activation of benzo(*a*)pyrene (BaP), β-naphthylamine, and protein pyrolysate products by primary human buccal mucosa epithelial cells.
Methods or Approach:
Primary cultures from human and rat buccal mucosa are established by conventional methods. After incubation with radioactive-labeled carcinogen for 24 hours, the binding level of carcinogen to DNA is determined as a measure of metabolic capabilities. The carcinogen-DNA adduct pattern and profile of BaP metabolites excreted into the media is determined by high performance liquid chromatographic analysis. Morphological changes after BaP treatment will also be investigated.
Results to Date:
Both fibroblast and epithelial cells derived from human buccal mucosa metabolize BaP into metabolites that react with mDNA. Level of carcinogen binding was two to three times as high in epithelial cells as in fibroblast cells derived from the same individual. No difference in BaP metabolite profile between the two cell types was observed. Treatment of an established rat tongue epithelial cell line with BaP (2 µg/mL) resulted in hyperkeratosis; however, high doses of BaP are required before a toxic effect is observed.
Future Plans:
The effect of cigarette smoke components on inducibility of aryl hydrocarbon hydroxylase and related enzymes in cultured human oral mucosa will be investigated.
Project Dates:
1984–1986.

0159. FREDERIKSSUND HOSPITAL, Surgical Department, Obstetric Ward, Copenhagen, Denmark.

Project Title:
Leucocyte Count and Smoking. Observations in Pregnant Women and Their Offspring at Birth.

Principal Investigators:
Asmussen, I,; Staun, P.
Objective:
To investigate the hypothesis that leukocyte count may be lower in heavy smokers (>10 cigarettes/day) than in nonsmokers.
Methods or Approach:
Questionnaires were completed at time of delivery that focused on maternal age, gestational age of child, pregnancy number, child sex and weight, and placental weight. Information was also collected on smoking habits. Leukocyte count was performed on venous blood drawn from the mother at delivery and from the umbilical vein of the newborn. Subjects were

healthy women who had had a normal pregnancy and who were expected to have an uncomplicated delivery.

Results to Date:
Of the 73 women who participated, 47 percent were daily smokers and 36 percent were heavy smokers. In this small sample, women pregnant for the first time were more often smokers than women planning a larger family. Leukocyte count paralleled number of cigarettes smoked (in both mother and child): a slight increase in leukocytes in light smokers and a marked decline in heavy smokers ($\geq$20 cigarettes/day). Smoking was also related to lower birth weight and lower placental weight in heavy smokers.

0160. GENTOFTE UNIVERSITY HOSPITAL, Department of Otolaryngology, 2900 Hellerup, Copenhagen, Sweden.

Project Title:
Goblet Cell Density in Human Bronchus in Chronic Bronchitis.

Principal Investigators:
Tos, M.; Moller, K.
Objective:
To determine the density of goblet cells in biopsies from normal people compared with densities in patients with chronic bronchitis.
Methods or Approach:
Using the whole mount method, 10 goblet cell counts of 0.01761 mm^2 were made on each of five biopsies (trachea, major bronchi, and lower lobe bronchi) for normal people and patients and mean density was calculated.
Results to Date:
A higher density of goblet cells was found in patients with bronchitis and in smokers compared with nonsmokers. The distribution of goblet cells was irregular, therefore only quantitative findings are of value.
Future Plans:
Goblet cell density in small bronchi of normal people (smokers vs. nonsmokers) will be determined.
Project Dates:
January 1982–May 1985.
Financial Support:
Gentofte Hospital.
Reference:
Tos, M.; Moller, K. "Goblet Cell Density in Human Bronchus in Chronic Bronchitis." *Archives of Otolaryngology* 673, 1983.

0161. INSTITUTE OF COMMUNITY HEALTH, Department of Social Medicine, J.B. Winslowsvej 17, DK-5000 Odense, Denmark.

Project Title:
Tobacco Use, Alcohol Consumption and Infertility.

Principal Investigators:
Olsen, J.; Rachootin, P.
Objective:
To study the association between alcohol consumption, tobacco use, and subfecundity.
Methods or Approach:
A case–control study was conducted using all women treated for infertility at Odense University Hospital during the period 1977 to 1980 as cases (1,069 women). The control group consisted of 4,305 women who had delivered a healthy child with a gestational age of over 258 days at the same hospital in the period 1977 to 1979.
Results to Date:
The relative risk of a conception delay of 1 year or more was 1.6 for smokers compared with nonsmokers. Use of tobacco and alcohol was significantly higher in cases compared with controls. For smokers, the relative risk of delayed conception in both a previous and current pregnancy was twice that of nonsmokers (significant at the 0.05 level).
Future Plans:
The effect of alcohol and smoking intervention on aggregated data will be studied.
Project Dates:
January 1981–1983.
Financial Support:
Institute of Community Health; Del laegevidenskabelige Forskningsrad (12-1712, 12-3352).
References:
(1) Olsen, J., Rachootin, P.; Schiodt, A.V. "Alcohol Use, Conception Time, and Birth Weight." *Journal of Epidemiology and Community Health* 37:63-65, 1983. (2) Olsen, J.; Rachootin, P.; Schiodt, A.V., et al. "Tobacco Use, Alcohol Consumption, and Infertility." *International Journal of Epidemiology* 12:179-184, 1983.

0162. ODENSE UNIVERSITY HOSPITAL, Department of Pediatrics, DK-5000 Odense C, Denmark.

Project Title:
Followup of the Odense Cohort of 1972-74.

Principal Investigator:
Ulrich, M.
Objective:
To study postnatal growth patterns in a population of Danish infants born in Odense between 1972 and 1974.
Methods or Approach:
Growth patterns are related to a number of factors, including maternal smoking during pregnancy. In the cohort of infants (already described), followups have been conducted at 6 months, 18 months, 2.5 years, and 6 years. Measurements have been made of height, weight, head circumference, and biparietal diameter.
Results to Date:
Evaluation of data is continuing.
Future Plans:
It is anticipated that the cohort will be followed up at 13 and 14 years of age.
Project Dates:
August 1972–1987.
Reference:
Ulrich, M. "Fetal Growth Patterns in a Population of Danish Newborn Infants." *Acta Paediatrica Scandinavica* Supplement 292:5-45, 1982.

0163. ROYAL DENTAL COLLEGE, UNIVERSITY HOSPITAL, Department of Oral Medicine and Oral Surgery, DK-2100 Copenhagen, Denmark.

Project Title:
Malignant Potential of Oral Lichen Planus.

Principal Investigators:
Holmstrup, P.; Thorn, J.; Lorup, J.R., et al.
Objective:
To obtain information on the potential for malignant transformation of oral lichen planus lesions over a 15-year period.
Methods or Approach:
A total of 700 patients with histologically verified oral lichen planus are being followed. The patients are asked about past

and present oral symptoms and smoking habits. The location and type of oral lichen planus lesions are registered and photographed. After the first examination, the patients with lingular lesions are seen once a year except for those with epithelial dysplasias who are seen every third month. In the followup examinations, all changes of the lesions are recorded, photographed, and, if necessary, biopsied. So far, eight patients have been found with a simultaneous occurrence of lichen planus and erythroplakia. The influence of smoking on the evaluation of lesions will be studied.

Results to Date:
Results are not yet available.

Project Dates:
1970–1985.

Financial Support:
WHO (D-IARC-79-132).

0164. UNIVERSITY HOSPITAL OF AARHUS, INSTITUTE OF CANCER RESEARCH, Department of Oncology and Radiotherapy, Norrebrogade 44, 8000 Aarhus C, Denmark.

Project Title:
An Epidemiological Case–Control Study of Bladder Cancer in a Predominantly Rural District of Denmark.

Principal Investigators:
Mommsen, S.; Aagaard, J.; Sell, A.

Objective:
To investigate the determinants of an increased relative risk (RR) of developing bladder cancer in a predominantly rural area.

Methods or Approach:
The cohort consisted of 165 male and 47 female bladder cancer patients matched with 165 male and 94 female controls. Subjects were interviewed about all known etiologic factors of bladder cancer. Results were evaluated by multivariate logistic analysis.

Results to Date:
All types of tobacco consumption (except pipe smoking), industrial work, prostatic hypertrophy, and possible saccharin consumption may all be of etiological importance for induction of bladder cancer.

Future Plans:
A case–control study of bladder cancer will be conducted, including histological identification of the urothelium in the pheriphery of the bladder mucosa in patients with prostatic hypertrophy.

Project Dates:
September 1977–1980.

Financial Support:
Danish Cancer Society, Laboratory of Environmental Carcinogenesis (M-7/80); MRC, Denmark.

0165. UNIVERSITY HOSPITAL, RIGSHOSPITALET, Dental Department, Tagensvej, DK-2200 Copenhagen, Denmark.

Project Title:
Cancer Development in Tobacco-Induced Oral Leukoplakias Associated With "Fingerprint-of-Tobacco" Changes.

Principal Investigator:
Pindborg, J.J.

Objective:
To study and compare differences in malignant potential of tobacco-induced oral leukoplakias with that observed in idiopathic leukoplakia.

Methods or Approach:
Patients are photographed and followed clinically and with biopsies.

Results to Date:
It appears that idiopathic oral leukoplakias are more inclined to turn into malignancy than the "fingerprint-of-tobacco" type.

Project Dates:
1970–continuing.

Financial Support:
Rigshospitalet, Denmark.

0166. UNIVERSITY OF AARHUS, INSTITUTE OF PHYSIOLOGY, 8000 Aarhus C, Denmark.

Project Title:
Changes in Static and Dynamic Ventilatory Parameters of Medical Students As Related to Age, Previous and Present Environmental Conditions, and Smoking Habits.

Principal Investigators:
Lyager, S.; Naeraa, N.; Olsen, C., et al.

Objective:
To (1) obtain a more precise picture of transition from growth-related increase in ventilatory parameters during adolescence to age-related decrease; (2) establish a set of normal reference values valid for adults aged 19 to 25 years; and (3) test which measured parameter is the most sensitive to age and smoking habits.

Methods or Approach:
A longitudinal study is being conducted (entering its fourth year in January 1985), in which each individual is examined every sixth month through the 3 years of premedical curriculum and, if possible, through the 3 clinical years of the medical curriculum of the university. On each occasion, body plethysmography is used to examine static lung volumes and midexpiratory flow volume curves are examined with air and helium. A questionnaire is used to follow subjective health status, including smoking habits.

Results to Date:
After the fifth examination of medical students aged 19 to 25, forced expiratory volume in 1 sec value had decreased below initial values in 67 percent of females and in 77 percent of males.

Project Dates:
November 1981–1987.

Financial Support:
University of Aarhus.

0167. UNIVERSITY OF AARHUS, INSTITUTE OF HYGIENE, Bygning 180, Universitetsparken, DK-8000 Aarhus C, Denmark.

Project Title:
Investigation of the Health Consequences of Exposure to Tobacco Dust With Regard to Threshold Limit Values.

Objective:
To relate concentration of tobacco dust to occurrence of acute and chronic illnesses among workers in the tobacco industry.

Methods or Approach:
The field study will involve a factory belonging to the Scandinavian Tobacco Co. along with the Telephone Company of Jutland (control) and will include (1) evaluation of indoor climatic conditions (dust production, ventilation, cleaning); (2) measurement of dust and organic gases and vapors; (3) physical, chemical, and biological characterization of collected dust samples; (4) medical examination (questionnaire, physical examination, lung function tests at different times during the

day and week, allergy tests); and (5) statistical analysis of results. Subjects include 75 tobacco workers and 50 control workers.

Results to Date:
Results are not yet available.

Future Plans:
A controlled exposure study will probably be conducted at the Institute of Hygiene to establish the dose–response relationship of tobacco dust exposure.

Project Dates:
February 1984–April 1985.

Financial Support:
Danish Working Environment Fund.

0168. UNIVERSITY OF COPENHAGEN, GLOSTRUP HOSPITAL, Faculty of Medicine, 2600 Glostrup, Copenhagen, Denmark.

Project Title:
1914 Population Study in Glostrup.

Principal Investigators:
Schroll, M.; Hagerup, L.

Objective:
To investigate risk factors for cardiovascular symptoms.

Methods or Approach:
A cohort of 975 men and women who were born in 1914 and living in the Glostrup hospital area in 1964 were invited to a health examination in 1964. Eighty-two percent participated. In 1974, survivors were reinvited and 666 participated (68 percent of those originally invited, 88 percent of the surviving former participants). In 1979, a register followup was performed regarding death and/or hospitalization. In 1964 and 1974, smoking habits were described in terms of inhalation, kind of tobacco, amount, duration of smoking, and changes over the decade. The health implications were then examined.

Results to Date:
After 10 years, tobacco consumption in this population was the most important risk factor for overall mortality, cardiovascular manifestations, peripheral arterial disease, decline in pulmonary function, and symptoms of ulcer. The relative risk of death, fatal and nonfatal cardiovascular manifestations, and decline in pulmonary function increased gradually with the amount of tobacco smoked. Inhalation roughly doubled the risk. The excess risk for pipe/cheroot smokers was less than that for cigarette smokers. Ex-smokers reduced their risk almost 100 percent. The risk associated with smoking was independent of other factors. The excess risk attributable to smoking was as great in women as in men, but the community problem of smoking-related diseases was most pronounced in men among whom smoking habits are more widely spread and morbidity is higher. The results from the 1914 population study suggest that almost one-third of all deaths and heart attacks in middle-aged Danes might be avoided if all 50-year-olds would become ex-smokers. Followup examination of the study population was done (1984, age 70).

Future Plans:
Analyses regarding a 15-year register followup is in progress.

Project Dates:
January 1964–continuing.

Financial Support:
Glostrup Hospital; MRC, Denmark (512-3304; 512-4167; 512-5729; 512-6714; 512-10272).

Reference:
Schroll, M. "Smoking Habits in the Glostrup Population of Men and Women, Born in 1914." *Acta Medica Scandinavica* 208(4):245-256, 1980.

0169. UNIVERSITY OF COPENHAGEN, LABORATORY FOR THE THEORY OF GYMNASTICS, August Krogh Institute, Universitetsparken 13, DK-2100 Copenhagen, Denmark.

Project Title:
Acute Effects of Cigarette Smoking and Inhalation of Carbon Monoxide During Maximal Exercise.

Principal Investigators:
Klausen, K.; Andersen, C.; Nandrup, S.

Objective:
To compare the acute effect of inhaling smoke of three cigarettes with effect of inhalation of an amount of carbon monoxide (CO) giving the same CO-saturation of arterial blood as smoking during rest and during maximal exercise on a Krogh cycle ergometer.

Methods or Approach:
Sixteen male subjects were tested in the morning (1) after about 8 hours without smoking (control), (2) after inhalation of the smoke of three cigarettes (smoking), and (3) after CO inhalation (CO).

Results to Date:
It was found that the average maximal rate of O_2 uptake (V_{O_2}) decreased during both smoking and CO by about 7 percent. Endurance time at V_{O_2} max decreased 20 percent during smoking but only 10 percent during CO inhalation. A significant decrease in maximal heart rate (HR), and an increase in HR at rest, was demonstrated only during smoking. The peak lactate concentration (HLa) following maximal exercise was significantly decreased after smoking. Results suggest that the decrease in V_{O_2} max during smoking is due to the CO saturation, and hence to a decrease in the oxygen capacity of the blood, while the decrease in endurance time during smoke is a combined effect of CO saturation and an increased cost of breathing caused by smoke particles. Also, nicotine (or other smoke components) may have an enhancing effect on the heart at rest, but inhibition is seen during maximal exercise. It was also found that subjects who had a V_{O_2} max above average were less susceptible to smoking effects than subjects with a below average level.

Financial Support:
Danish Sports Research Council.

Reference:
Klausen, K.; Andersen, C.; Nandrup, S. "Acute Effects of Cigarette Smoking and Inhalation of Carbon Monoxide During Maximal Exercise." *European Journal of Applied Physiology* 51:371-379, 1983.

0170. UNIVERSITY OF COPENHAGEN, Copenhagen, Denmark. UNIVERSITY OF BERGEN, Bergen, Norway.

Project Title:
Pinocytotic Activity in Smokers Endothelium.

Principal Investigators:
Asmussen, I.; Svendsen, E.

Objective:
To test already available material, using a double-blind technique, for pinocystotic activity.

Methods or Approach:
Material consisted of umbilical arteries, umbilical veins, and placental capillaries from 52 women (22 smokers of >10 cigarettes/day) and 30 nonsmokers. There were 156 specimens for the study of endothelial cell pinocystotic activity. Electromicroscopy had been performed and data had been used to study the effect of smoking on the human vascular wall.

Micrographs showing endothelial cells were selected for the morphometric study and sent to Bergen under coding.
Results to Date:
Project is in progress, but data are not yet available.

0171. UNIVERSITY OF COPENHAGEN, Copenhagen, Denmark.

Project Title:
Mitochondrial Proliferation in Smokers Endothelium.

Principal Investigator:
Asmussen, I.
Objective:
To describe morphological changes in mitochondria size and number in smokers endothelium.
Methods or Approach:
Materials used were from 22 heavy smokers (>10 cigarettes/day) and 30 nonsmokers. Umbilical arteries were studied with electron microscopy using a blind-doubleblind technique.
Results to Date:
An increased number of mitochondrial profiles was observed in many endothelial cells from smokers; mean 23/endothelial cell compared with 3/cell in nonsmokers. Mitochondrial volume density ranged from 0.15 to 0.62 in smokers and from 0.01 to 0.02 in nonsmokers. Mitochondrial index was 0.008 to 0.060 (mean 0.018) in smokers and 0.003 to 0.008 (mean 0.006) in nonsmokers. Thus, in smokers, a larger area of the endothelial cell cytoplasm was often occupied by mitochondria, and smokers had a greater number of mitochondrial profiles, but mean size of mitrochondria (profiles) was only slightly increased. Mitochondria may proliferate within cells, and results seems to indicate that smoking may be a growth factor for mitochondria. A similar study in diabetics found no signs of mitochondrial proliferation.
Reference:
Asmussen, I. "Mitochondrial Proliferation in Endothelium. Observations on Umbilical Arteries From Newborn Children of Smoking Mothers." *Atherosclerosis* 50(2):203-208, February 1984.

0172. UNIVERSITY OF COPENHAGEN, RIGSHOSPITALET, Copenhagen, Denmark.

Project Title:
Severe Lifethreatening Atherosclerotic Lesions in Neck, Abdominal Arteries and Lower Limbs. A Study of Risk Profile.

Principal Investigator:
Asmussen, I.
Objective:
To study importance of tobacco smoking as a risk factor in peripheral atherosclerosis with respect to localization, area of debut, type of lesion, and coexisting coronary heart disease.
Methods or Approach:
The study cohort consisted of patients admitted consecutively during a 6-month period for vascular surgery. A questionnaire about various risk factors for development of atherosclerosis was administered with special focus on smoking habits (including initiation of smoking).
Results to Date:
Among patients, 18 percent were <50 years of age, and of these 76 percent were admitted for the first time. Among women below age 50, 47 percent were readmitted for vascular surgery. At time of admission, even in groups below age 50, many had symptoms of severe atherosclerotic lesions lasting for >5 years, some for >10 years. Coronary heart disease coexisted with peripheral atherosclerosis in 37 percent (17 percent of women and 83 percent of men). In 15 percent, onset of coronary artery disease was before age 50. Only five patients (all older women) claimed to be nonsmokers (never smokers). All patients <50 years of age were heavy smokers. Among women, 25 percent had taken up smoking before the age of 15; among men, 65 percent had started smoking before 15 years of age. Most patients smoked cigarettes. In cigar and cheroot smokers, massive calcifications were found both at angiography and at surgery. Arteries in these smokers (even abdominal aorta and iliac arteries) were transformed into heavily calcified tubes.

EGYPT

0173. CAIRO UNIVERSITY, CANCER INSTITUTE, 11 Boulos Hanna Street, Dokki, Cairo, Egypt.

Project Title:
Assessment of Smoking Prevalence in Egypt.

Principal Investigator:
Omar, S.
Objective:
To (1) assess prevalence of smoking among different target groups; (2) assess tobacco yield in local and imported cigarettes and in locally used "Hubble Bubble"; (3) assess different approaches used in antismoking campaigns; and (4) conduct antismoking actions.
Methods or Approach:
Targeted groups include medical professionals, teachers, students, members of the armed forces, and athletes. The use of antismoking materials (such as posters) and religious approaches during campaigns are evaluated, in addition to response to antismoking legislation. The WHO/UICC questionnaire is used in surveys and results are analyzed by computer. Educational programs are organized and evaluated. Tobacco samples, randomly selected from all over the country, are assessed (with control samples).
Results to Date:
Data indicate that 39.8 percent of males but only 0.9 percent of females are current smokers; however, average per capita consumption has increased 133.3 percent since 1970. Among target groups, the proportion of male smokers was highest in the armed forces (51.1 percent) and lowest among athletes (18.5 percent). Proportions for male doctors and teachers were 46.8 and 45.4 percent, respectively. The highest proportion of female smokers (9.9 percent) was found among teachers. Over 70 percent of smokers among doctors, teachers, and members of the armed forces smoked ≥20 cigarettes/day; among the few athletes who smoked, 46.4 percent smoked ≥20 cigarettes/day. An organized antismoking program for a sample of members of the armed forces produced changes in attitudes and smoking behavior. Religious and social components of the program were the most influential in changing attitudes. More than half of the participants also reduced daily consumption

(35.0 percent) or quit smoking (15.3 percent). A poster campaign was not as successful; 66 percent of smokers surveyed who saw the posters daily responded negatively and did not change smoking attitudes. In 1973, respiratory cancer ranked fifth in the order of most frequent sites of cancer in males; by 1978, it was ranked third. Levels of tar and nicotine in Egyptian cigarettes are being reduced, based on a new law that stipulates maximum levels. In 1981, the popular Cleopatra brand (17 mm filter) contained 21.9 mgm tar and 1.9 mgm nicotine; in January 1984, levels had dropped to 17.2 and 1.1 mgm, respectively. Similar reductions were found for other popular brands.

Future Plans:
Emphasis will be placed on studying the problem of smoking in the medical professions, conducting educational programs, arranging cessation kits to be provided to doctors, and increasing activities among the armed forces.

Project Dates:
August 1982–December 1985.

Financial Support:
WHO.

Reference:
Omar, S.; Hussein, M.; Ebeid, N., et al. "Prevention of the Smoking Epidemic in a Developing Country - Egypt. A Review Paper." *Armed Forces Medical Journal* 27(2):136-146, 1984.

FEDERAL REPUBLIC OF GERMANY

0174. ACADEMY OF SCIENCE AND LITERATURE, D-6500 Mainz, Federal Republic of Germany. UNIVERSITY OF MAINZ, INSTITUTE FOR PHYSIOLOGICAL CHEMISTRY, Duesbergweg, D-6500 Mainz, Federal Republic of Germany.

Project Title:
Assessment of Age Correlated Alterations of the Primary Information Carrier, the DNA.

Principal Investigators:
Zahn, R.K.; Mueller, W.E.G.

Objective:
To measure DNA alterations, especially single-strand breaks; conduct factor analyses of large populations leading to isolation of important factors bearing on age correlations, such as smoking habits or dietary preferences.

Methods or Approach:
DNA alterations following treatment with alkali or different single-strand specific nucleases give rise to single-strand breaks, called single-strand events (SSE). Experiments will include (1) isolation of DNA from small samples of post-mitotic tissues (muscle from humans of different ages); (2) treatment with different SSE-specific nucleases such as Nuclease S_1 from *Apergillus oryzae*, Nuclease BAL 31 from *Alteromonas espejiana* and Pea Endonuclease from *Pisum sativum* causing cuts in intact DNA strand and giving rise to shorter double-stranded DNA pieces; and (3) measurement of piece length by following the molecular contour with a stylo on an electrostrictive pad. Impulses are evaluated with the aid of a computer.

Results to Date:
The multiple correlation of age vs. molecular weight and standard deviation differed between nonsmokers and heavy smokers, where the decrease of molecular weight and standard deviation is steeper. In 267 people (undefined smoking, dietary, and drug use habits) evaluated for SSE, a clear age dependence in the decrease of undamaged DNA length is shown with an increase in the standard deviation with age.

Project Dates:
1972–1988.

Financial Support:
Academy of Science and Literature, Federal Republic of Germany.

0175. DEUTSCHES KREBSFORSCHUNGSZENTRUM, INSTITUTE OF TOXIKOLOGIE UND CHEMOTHERAPIE, D-6900 Heidelberg, Federal Republic of Germany.

Project Title:
Relevance of Gas and Particulate Phases of Tobacco Smoke for Bronchial Cancer Formation. An Experimental Study in Syrian Golden Hamsters.

Principal Investigators:
Zeller, W.J.; Schmahl, D.; Ivankovic, S.

Objective:
To determine whether the lower boiling constituents of the gas phase of cigarette smoke such as acrolein, hydrogen cyanide, and formaldehyde, which are ciliatoxic, can inhibit the self-purifying capacity of the bronchi and thus act as pacemakers for penetration of carcinogens such as hydrocarbons; determine whether filtration of the ciliatoxic compounds by means of carbon filters can protect against the carcinogenic activity of hydrocarbons.

Methods or Approach:
To elucidate the hypothesis, benzo(*a*)pyrene (BaP) was instilled intratracheally (in addition to chronic smoke inhalation) in Syrian golden hamsters. Two experiments were performed. In the first, using plain cigarettes, a Cambridge filter and carbon trap were mounted in the course of the smokestream between the smoke chamber and inhalation chamber of a Hamburg type II smoking machine. In the second, filter-tipped cigarettes (acetate filter or carbon-containing acetate filter) were used. Period of smoke inhalation was 50 and 73 weeks in experiments I and II, respectively, on an inhalation schedule of 2 x 30 cigarettes/day. Total dose of BaP was 10.5 mg/animal in experiment I and 10.0 mg/animal in experiment II.

Results to Date:
In both experiments, pathologic changes following smoke inhalation and BaP instillation were reduced by 50 percent and 40 percent, respectively, in groups in which smoke was passed through an additional carbon filter compared with groups exposed to smoke not passed through the filter. In experiment I, reduction was due mainly to a significantly lower yield of carcinomas; in experiment II, reduction in the number of metaplasias, papillomas, and adenomas was observed.

Project Dates:
1975–1983.

Financial Support:
Deutsches Krebsforschungszentrum, Federal Republic of Germany.

0176. GSF RESEARCH CENTER, INSTITUTE FOR MEDICAL INFORMATION AND HEALTH SERVICES RESEARCH (MEDIS), Department of Epidemiology, Ingolstadter Landstrasse 1, D-8042 Neuherberg bei Munchen, Federal Republic of Germany.

Project Title:
MONICA (Monitoring of Trends and Determinants in Cardiovascular Disease) Project Augsburg.

Principal Investigator:
Keil, U.

Objective:
To measure trends in cardiovascular mortality and coronary heart disease and cerebrovascular morbidity; assess extent to which trends are related to changes in known risk factors, daily living habits, health care, or major socioeconomic features measured at the same time in defined communities in different countries (or centers).

Methods or Approach:
MONICA is coordinated by the World Health Organization in Geneva; MONICA Augsburg is 1 of approximately 30 centers. All fatal and nonfatal myocardial infarction events (inside or outside hospitals) will be monitored for 10 years in the Augsburg region (approximately 530,000 people). Three independent surveys will be conducted: at the beginning, in the middle, and at the end of the 10-year period. The first survey, to be completed in May-June 1985, will be based on a random population sample (5,312) from the Augsburg region. The MONICA survey instrument incorporates an extensive series of questions on smoking.

Results to Date:
Preliminary results will be available by the end of 1985.

Future Plans:
The first MONICA survey will be transformed into a cohort study and carried out over a period of at least 10 years.

Project Dates:
October 1984–1994.

Financial Support:
Ministry for Research and Technology, Bonn; GSF, Neuherberg, Federal Republic of Germany.

Reference:
Fricke, H.; Keil, U. *The Munich Blood Pressure Program (MBP).* Volume 1a, Munich, Institute for Medical Information and Health Services, June 1983, 25 pp.

0177. GSF, NEUHERBERG, Abt. F. Strahlenbiologie, Zytogenetik, D-8042 Munich-Neuherberg, Federal Republic of Germany.

Project Title:
Cytogenetic Effects of Environmental Chemicals.

Principal Investigator:
Bauchinger, M.

Objective:
To conduct biological monitoring of persons occupationally or ecologically exposed to enviromental chemicals; determine whether smoking exerts a synergistic effect.

Methods or Approach:
Chromosome analysis was conducted on lymphocytes from workers at a plant producing pentachlorophenol (PCP) and among workers occupationally exposed for more than 20 years to 50 Hz alternating electric and magnetic fields in 380 kV switchyards.

Results to Date:
There was no significant increase in sister chromatid exchanges (SCEs) in PCP workers compared with smokers in a control group. Workers did show a small, but significant, increase in frequency of dicentrics and acentrics. In contrast to SCE data, significantly higher aberration yields were present in smoking PCP workers than in controls who smoked. In the control group, smokers had a higher incidence of SCEs than nonsmokers. Smoking also had no significant effect of frequency of SCEs in workers exposed to electric and magnetic fields. Neither the yields of structural chromosome changes nor SCE frequencies were increased in workers (smokers and nonsmokers) compared with controls.

Future Plans:
The effect of formaldehyde exposure will be investigated.

Project Dates:
September 1984–March 1985.

Financial Support:
GSF, Neuherberg, Federal Republic of Germany.

References:
(1) Bauchinger, M.; Hauf, R.; Schmid, E., et al. "Analysis of Structural Chromosome Changes and SCE After Occupational Long-Term Exposure to Electric and Magnetic Fields From 380 kV-Systems." *Radiation and Environmental Biophysics* 19(4):235-238, 1981. (2) Bauchinger, M.; Dresp, J.; Schmid, E., et al. "Chromosome Changes in Lymphocytes After Occupational Exposure to Pentachlorophenol (PCP)." *Mutation Research* 102(1):83-88, 1982.

0178. JOHANNES GUTENBERG UNIVERSITY, ACADEMY OF SCIENCE AND LITERATURE, Institute for Physiological Chemistry, Geschwister-Scholl-strasse 2, D-6500 Mainz, Federal Republic of Germany.

Project Title:
Fast Effect of Tobacco Smoke Condensate.

Principal Investigators:
Zahn, R.K.; Stueber, J.J.

Objective:
To evaluate DNA alterations, DNA repair, and repair modulation in the presence of tobacco smoke fractions.

Methods or Approach:
Condensate is derived from a smoking machine and fractionated for elimination of water soluble components. Condensate effects are tested in tissue culture with mouse lymphoma celss, Friend leukemia cells, and different organisms, by alkaline elution and electron microscopic evaluation. Absolute numbers of single-strand breaks (SSE, single-strand events) in DNA are evaluated and dose relationships established of events within 20 minutes to 2 hours. Disappearance of SSE within 90 minutes to from 3 to 4 hours is followed. Using methyl-nitronitrosoguanidine or other DNA-damaging agents, predictable numbers of SSE are provoked and their disappearance is studied in the presence of environmental poisons and tobacco smoke condensate fractions.

Results to Date:
Measurements clearly show that tobacco smoke condensate fractions contain high concentrations of DNA damaging substances (using equivalent of 0.1 to 1.0 cigarette puff as dose for one analysis).

Project Dates:
April 1984–1988.

Financial Support:
University of Mainz, Federal Republic of Germany.

0179. KLINIK LOEWENSTEIN, D-7101 Loewenstein, Federal Republic of Germany.

Project Title:
Obligatory Smoking Cessation Program for Patients Who Want To Be Treated at Klinik Loewenstein.

Principal Investigators:
Krause, F.; Freigang, W.F.
Objective:
To conduct a behavioral modification program for smoking cessation among all patients who smoke and are seeking treatment at a lung disease clinic.
Methods or Approach:
During the 14-day program, participants meet daily and report about their experiences with smoking cessation. No patients are operated on unless they have stopped smoking.
Results to Date:
Since the program was started in November 1984 (3 months), two courses have been conducted and 10 patients have stopped smoking, a cessation rate of about 40 to 50 percent, which is similar to rates found for other such courses. It has been found that approximately 30 percent of patients that stop smoking before an operation resume smoking at a later date.

0180. MEDIZINISCHE UNIVERSITATS-KLINIK, Abteilung Pulmologie, Hugstetterstrasse 55, D-7800 Freiburg, Federal Republic of Germany.

Project Title:
Surface Markers on Lymphocytes and Macrophages in Bronchoalveolar Lavage Fluid and Blood From Smokers and Nonsmokers.

Principal Investigators:
Costabel, U.; Matthys, H.; Bross, K J.
Objective:
To (1) detect abnormalities in immunoregulatory T-cells in bronchoalveolar lavage fluid of smokers; (2) analyze surface markers on macrophages to correlate them with functional status of cells; and (3) determine whether an imbalance of immunoregulatory lymphocytes and dysfunction of immunological status of macrophages in lungs of smokers plays a role in local host defense and carcinogenesis.
Methods or Approach:
Bronchoalveolar lavage cells and peripheral blood are collected from nonsmokers and asymptomatic smokers. Cells are stained for surface markers by monoclonal antibodies using the peroxidase-antiperoxidase method performed on glass slides. Evaluation is carried out with a light microscope by counting at least 200 cells for each marker. A battery of commercially available monoclonal antibodies against lymphocyte subpopulations and macrophage surface antigens is applied.
Results to Date:
The ratio of T-helper/inducer cells to suppressor/cytotoxic cells is significantly reduced in BAL, but not in blood, of light to moderate younger cigarette smokers compared with nonsmokers.
Future Plans:
The study will be extended to include smokers with chronic bronchitis with or without concomitant airways obstruction and patients with carcinoma of the lung.
Project Dates:
October 1983–April 1987.
Financial Support:
Duetsche Forschungsgemeinschaft (Co 118/2-1).

0181. PNEUMOCONIOSES RESEARCH INSTITUTE, Hunscheidtstrasse 12, 4630 Bochum 1, Federal Republic of Germany.

Project Title:
Influence of Smoking Habits on the Production of Histamine and Leukotriene in the Bronchial Tree.

Principal Investigators:
Ulmer, W.T.; Schlosser, K.
Objective:
To determine if smoking habits influence the production of leukotrienes in the bronchial tree.
Methods or Approach:
Leukotrienes play an important role in diseases such as asthma and may be implicated in chronic bronchitis. The investigation will measure histamine by a fluorometric method and leukotrienes by high performance liquid chromatography in sputa and bronchial lavage fluid.
Results to Date:
Project is in a preliminary phase.
Project Dates:
March 1985–December 1986.
Financial Support:
Tobacco Industry Panel.

0182. PNEUMOCONIOSES RESEARCH INSTITUTE, Hunscheidtstrasse 12, 4630 Bochum 1, Federal Republic of Germany.

Project Title:
Influence of Smoking on the Incidence of Chronic Obstructive Airway Disease.

Principal Investigators:
Ulmer, W.T.; Staguhn, M.
Objective:
To determine influence of smoking on development of airway obstruction.
Methods or Approach:
A relationship between smoking and bronchitis and chronic bronchitis has been shown, but it is still not clear whether obstructive bronchitis is related to smoking. All clinic patients were examined for amount of airway obstruction, and smoking habit information was recorded. A group of outpatients served as controls.
Results to Date:
Data have been collected and are bing analyzed. Final results are not yet available.
Project Dates:
September 1982–March 1985.
Financial Support:
Pneumoconioses Research Institute.

0183. RESEARCH LABORATORIE, Goethestrasse 20, D-8000 Munich 2, Federal Republic of Germany.

Project Title:
Metabolic Aspects of Smoking Behavior.

Principal Investigator:
Schievelbein, H.
Objective:
To determine how white blood cell metabolism may be changed by smoking; determine which smoke components cause the changes.
Methods or Approach:
Habitual smokers will consume various brands of cigarettes that differ in nicotine and total particulate content. Blood

samples will be studied to find parameters of leukocyte metabolism.

Results to Date:
Results are not yet available.

Financial Support:
Committee on Smoking and Health, Federal Republic of Germany

0184. UNIVERSITAT FREIBURG, ANATOMISCHES INSTITUT, D-7800 Freiburg im Breisgau, Federal Republic of Germany.

Project Title:
The Effects of Maternal Smoking on the Neonatal Umbilical Cord.

Principal Investigators:
Staubesand, J.; Seydewitz, V.; Hugod, C., et al.

Objective:
To establish whether or not degenerative changes found in the umbilical cords of newborn children may be attributed to the smoking habits of the mother.

Methods or Approach:
Umbilical cords were obtained from infants of 31 mothers and labeled for further "blind" handling. The women were divided into three groups: nonsmokers, light smokers (≤ 15 cigarettes/day during pregnancy), and heavy smokers (≥ 15 cigarettes/day during pregnancy). Blood vessels of the cord were examined under the electron microscope and strict precautions were taken to eliminate effects of irrelevant factors. The fixation method was the subject of a separate experiment.

Results to Date:
Data do not confirm the suggestion that changes in cord blood vessels similar to those of atherosclerosis are brought about by maternal smoking during pregnancy. Pathological changes in the cord at term may be found in infants of healthy, nonsmoking mothers, and differences due to variations in fixation technique or to differences in duration or difficulty of labor cannot be disregarded.

Future Plans:
Experiments will be carried out on the cords of newborns delivered by caesarean section.

Reference:
Staubesand, J.; Hugod, C.; Mau, G., et al. "Intimal Ultrastructural Morphology of Umbilical Cord Vasculature in Babies Born to Cigarette Smoking Mothers." *VASA* 13(2):138-146, 1984.

0185. UNIVERSITY HOSPITAL, FIRST MEDICAL CLINIC, Martinistrasse 52, 2000 Hamburg 20, Federal Republic of Germany.

Project Title:
What Substances in Tobacco Are Responsible for the Epidemics of Smoking-Related Diseases?

Principal Investigators:
Doerken, H.; Heicke; Weller.

Objective:
To investigate carcinogens (particularly arsenic), circulatory toxins, and active virus particles (tobacco mosaic virus) in tobacco that may be factors in smoking-related diseases.

Methods or Approach:
Analysis will be made of various brands of tobacco to determine arsenic levels (by atomic absorption spectroscopy); and biological tests will be used to determine levels of tobacco mosaic virus in tobacco.

Results to Date:
Current data show that the arsenic content of Western and Chinese cigarettes is surprisingly high (30 brands studied) while the virus is seldom recovered in Chinese cigarettes.

Project Dates:
1984–1986.

0186. UNIVERSITY OF HEIDELBERG, INSTITUTE OF PATHOLOGY, Im Neuenheimer Feld 220, D-6900 Heidelberg, Federal Republic of Germany.

Project Title:
Smoking Habits Among Lung Cancer Patients; Correlation to Tumor Type and Mortality.

Principal Investigators:
Kayser, K.; Bulzebruck, H.; Shaver, M.

Objective:
To examine influence of smoking on postoperative complications after lung resection for bronchial carcinoma with regard to tumor type, differentiation, and tumor stage.

Methods or Approach:
Data on smoking habits is provided in patient records through use of standardized questionnaire on "History and Lifestyle." Findings will be compiled in a data bank and correlated with tumor type, differentiation, postoperative complications (retention pneumonia, emphysema), and mortality. Followup will be conducted to determine tumor recurrence and survival rates.

Results to Date:
Data are being compiled for the 120 patients analyzed. Preliminary analysis indicated that smoking influences postoperative complications. Short-term survival is better in heavy smokers than in nonsmokers; however, long-term survival is better in nonsmokers than in heavy smokers.

Future Plans:
Information will be collected and analyzed until statistics are significant ($p \leq 0.05$).

Project Dates:
February 1982–December 1985.

Financial Support:
University of Heidelberg.

0187. UNIVERSITY OF HEIDELBERG, INSTITUTE OF PATHOLOGY, Im Neuenheimer Feld 220, D-6900 Heidelberg, Federal Republic of Germany.

Project Title:
Influence of Smoking, Alcohol, and Pollution in Lung Carcinoma Patients.

Principal Investigators:
Kayser, K.; Bulzebruck, H.; Shaver, M., et al.

Objective:
To evaluate known influence of smoking, and possible influence of air pollution in carcinogenesis or lung carcinoma; examine hazards of smoking, air pollution in area of residence, alcohol consumption for lung carcinoma by cell type.

Methods or Approach:
Lung cancer patients, treated at the hospital of thoracic surgery, will be questioned about smoking and drinking habits and the time period lived at last place of residence. Residential area will be evaluated for air pollution due to traffic, nitrogen oxides, sulfur dioxide, and dust. Additional chronic lung diseases (bronchitis, emphysema) and tumor cell type will be included. Regression and multivariate analyses will be performed.

Results to Date:
More than 450 patients have been selected; data collection and analysis is under way.
Future Plans:
Project will be extended if data indicate that air pollution influences carcinogenesis.
Project Dates:
September 1984–September 1985.
Financial Support:
University of Heidelberg.

0188. UNIVERSITY OF HEIDELBERG, Research Department on Preventive Oncology, D-6800 Mannheim, Federal Republic of Germany.

Project Title:
Examination of Lung Function in 1,000 Smoking and Nonsmoking Pupils of Vocational Schools in Mannheim.

Principal Investigators:
Haussmann, R.; Schmidt, F.
Objective:
To determine if functional lung damage from smoking can be detected in relatively young smokers.
Methods or Approach:
Lung function of 1,000 smoking and nonsmoking pupils of vocational schools was examined by "Spirotron 2," a new measuring apparatus from Drager-Werke, Lubeck.
Results to Date:
Statistically significant changes in lung function were found among smokers in this young population.
Project Dates:
January 1984–1985.
Financial Support:
University of Heidelberg.

0189. UNIVERSITY OF HEIDELBERG, CLINICAL FACULTY MANNHEIM, Department of Preventive Oncology, Maybachstrasse 14-16, D-6800 Mannheim, Federal Republic of Germany.

Project Title:
Comparison of the Frequency of Cervix Carcinoma in Smoking and Nonsmoking Females.

Principal Investigators:
Huber, E.; Schmidt, F.
Objective:
To determine frequency of cervical cancer in women who smoke; examine the relationship and possible causes.
Methods or Approach:
Questionnaires will be used to obtain information, which will be statistically analyzed.
Results to Date:
Data suggest that there is a statistical relationship between smoking and frequency of cervical cancer in women.
Project Dates:
1984–1985.
Financial Support:
University of Heidelberg.

0190. UNIVERSITY OF MAINZ, Department of Toxicology, Obere Zahlbacher Strasse 67, D-6500 Mainz, Federal Republic of Germany.

Project Title:
Metabolic Fate and Toxicological Significance of Dihydrodiols Derived From Polycyclic Aromatic Hydrocarbons Occurring in Cigarette Smoke.

Principal Investigator:
Oesch, F.; Platt, K.L.
Objective:
To establish the relative importance of metabolically formed dihydrodiols of polycyclic aromatic hydrocarbons (PAH) from cigarette smoke in the pathway that leads to cancer.
Methods or Approach:
Study methodology was to (1) synthesize a large number of dihydrodiols, catechols, and quinones of many different PAHs to find answers that are not restricted to one PAH but to the whole class of PAHs; (2) investigate the ability of these compounds to serve as substrates for enzymes that are known to play an important role in the metabolism of PAH and for enzymes that are less extensively studied, e.g., dihydrodiol dehydrogenase and carbonyl reductase; (3) study DNA binding of synthetic derivatives using a fluorometric method previously applied; and (4) attempt to modulate mutagenicity by supplying the test system with compounds that either modify activity of relevant enzymes or act as scavengers of reactive metabolites, or of reactive oxygen species.
Results to Date:
To date, 25 K-region and non-K-region *trans*-dihydrodiols, 14 catechols, and 28 *o*-quinones of PAH have been successfully synthesized. Since very little is known about the biochemical and biological behavior of *o*-quinones, possible metabolites of PAH, investigations were concentrated on this class of compounds. K-region *o*-quinones are very efficiently reduced by carbonyl reductase of human liver. Some of these *o*-quinones were even better substrates than ubiquinone-1, the best endogenous substrate of carbonyl reductase that is known. Bacterial mutagenicity tests of synthetic TII o-quinones revealed that again many of the K -region *o*-quinones could be metabolically activated to potent mutagens while all non-K-region *o*-quinones except two were inactive. However, some non-K-region *o*-quinones were highly cytotoxic. The most interesting result of the mutagenicity test of the *trans*-dihydrodiols was activation of the K-region dihydrodiols of dibenz(*a,h*)anthracene and picene to stong mutagens. Thus, besides the well-established activation to dihydrodiol bay-region epoxides, K-region dihydrodiols can also be precursors of potent mutagens. In the subcutaneous carcinogenicity test, only dibenz(*a,h*)anthracene-3,4-dihydrodiol, the non-K-region dihydrodiol that can be metabolically transformed to a bay-region epoxide, was carcinogenic. Interestingly, one of the phenols tested, 5-hydroxydibenz(*a,h*)anthracene, was also biologically active in this test. The three K-region *o*-quinones of dibenz(*a,h*)anthracene and picene were not carcinogenic.
Future Plans:
After completing synthesis of the large number of biologially interesting derivatives of PAH, investigations of DNA-binding, mutagenicity and carcinogenicity of *trans*-dihydrodiols and biologically related compounds will be pursued. Owing to the interesting biochemical and biological results obtained with K-region quinones, studies will concentrate on DNA-binding and mutagenesis of this class of compounds.
Project Dates:
January 1982–December 1982.
Financial Support:
CTR (1097D).

0191. VERBAND DEUTSCHER RENTENVERSICHERUNGSTRAGER, Eysseneckstrasse 55, 6000 Frankfurt am Main, Federal Republic of Germany.

Project Title:
Model Trial of Smoking Cessation Treatment.

Principal Investigator:
Schuntermann, M.F.

Objective:
To ascertain whether three selected smoking cessation methods could effectively change attitudes toward smoking in the long term; determine which method is the most effective.

Methods or Approach:
The three methods used were self-control, group therapy, and Bad Nauheim. In selected rehabilitation facilities, smokers at risk (> 10 cigarettes/day) suffering from chronic bronchitis or cardiovascular and rheumatic diseases and undergoing treatment, participate in group therapy. Medical, psychological, and sociological data are obtained by questionnaires at the beginning, during, and following treatment, and three times during 2-year followup. Approximately 5,000 persons are expected to participate, and there will be a control group that will not receive cessation therapy.

Results to Date:
Results for a subsample of patients show that short-term effectiveness (percentage of nonsmokers at end of treatment) depends heavily on interaction of treatment and medical indication. The only effective methods for patients with rheumatic disease were the Bad Nauheim method (24.3 percent) and self-control therapy (28.6 percent); among controls, cessation success was 9.5 percent. For chronic bronchitis, the Bad Nauheim method was most successful (32.2 percent vs. 19.9 percent for controls). No method showed a significant effect among patients with coronary heart disease and hypertension compared with controls (coronary heart disease 36.2 percent, hypertension 20.0 percent). With respect to long-term effectiveness (change in smoking behavior from end of treatment through 2-year followup), there is no evidence that smoking cessation treatment methods lead to more "negative" changes compared with controls.

Project Dates:
1977–1984.

Financial Support:
Verband Deutscher Rentenversicherungstrager.

FINLAND

0192. HELSINKI UNIVERSITY CENTRAL HOSPITAL, Department of Obstetrics and Gynecology, Haartmaninkatu 2, 00290 Helsinki 29, Finland.

Project Title:
Effects of Smoking on Maternal and Fetal Hemodynamics.

Principal Investigators:
Lehtovirta, P.; Forss, M.; Kariniemi, V., et al.

Objective:
To determine the acute effects of maternal smoking on maternal and heart rate variability (interval and differential indices).

Methods or Approach:
Fetal hemodynamic responses to tobacco smoke or its components were measured using abdominal electrocardiography. Fetal heart rate variability was computed by a special purpose microprocessor-based system that produces two indices of variability, differential index (DI) and interval index (II). II is primarily a measure of fetal arousal level and DI of fetal oxygenation. Intervillous placental blood blow was estimated by an intravenous ^{133}xenon method. Nicotine effects on fetomaternal hemodynamics were studied by giving nicotine chewing gum to mothers. Effects of carbon monoxide or other agents of nicotine-free smoke were tested in pregnant women by supplying herbal cigarettes.

Results to Date:
Smoking had similar acute effects on maternal hemodynamics in the second and third trimester; heart rate and blood pressure increased. Fetal response in the second trimester (which differed from the third) included an acute decrease in II but but no effect on DI; fetal heart rate increased. In the third trimester, II and DI decreased but fetal heart rate remained unchanged. It is suggested that the midtrimester fetus shows the narcotic effect (decrease of II) of one cigarette, as does the term fetus, but fails to show the hypoxic effect (decrease of DI), which has been observed in the term fetus. Nicotine gum (2 mg) caused increases in maternal blood pressure and heart rate in both trimesters, as did smoking. In the second trimester both the gum and smoking elevated fetal heart rate but in the third trimester, the gum decreased fetal heart rate in contrast with smoking, which had no effect. Smoking an herbal cigarette caused a transient increase in maternal blood pressure and heart rate in both trimesters, changes observed only during smoking. Smoking an herbal cigarette had no effect on fetal heart rate and no depressant effect on fetal heart rate variability (DI, II); the only response was a transient increase 5 to 10 minutes after smoking in the second trimester. It is concluded that nicotine seems to be responsible for the depressant effect of tobacco smoke on the fetus. The different responses of the differential index and baseline fetal heart rate to tobacco smoking and chewing nicotine gum at different stages of gestation remain unexplained. Smoking also caused an acute decrease in intervillous placental blood flow. When intervillous placental blood flow increased after smoking, both indices seemed to follow, DI more closely ($p < 0.001$) than II ($p < 0.01$).

Project Dates:
January 1978–continuing.

Financial Support:
Helsinki University Central Hospital.

References:
(1) Lehtovirta, P.; Forss, M.; Rauramo, I., et al. "Acute Effects of Nicotine on Fetal Heart Rate Variability." *British Journal of Obstetrics and Gynaecology* 90:710-715, 1983. (2) Forss, M.; Lehtovirta, P.; Rauramo, I., et al. "Midtrimester Fetal Heart Rate Variability and Maternal Hemodynamics in Association With Smoking." *American Journal of Obstetrics and Gynecology* 146:693-695, 1983. (3) Rauramo, I.; Forss, M.; Kariniemi, V., et al. "Antepartum Fetal Heart Rate Variability and Intervillous Placental Blood Flow in Association with Smoking." *American Journal of Obstetrics and Gynecology* 146:967-969, 1983. (4) Kariniemi, V.; Lehtovirta, P.; Rauramo, I., et al. "Effects of Smoking on Fetal Heart Rate Variability During Gestational Weeks 27 to 32." *American Journal of Obstetrics and Gynecology* 149:575-576, 1984.

0193. HELSINKI UNIVERSITY, Departments of Obstetrics and Gynecology and Public Health Science, Haartmaninkatu 2, SF-00290 Helsinki, Finland.

Project Title:
Effect of Smoking on the Fetal Coronary Arteries.

Principal Investigators:
Lehtovirta, P.; Pesonen, E.; Sarna, S.
Objective:
To find the possible first observable changes in the fetal coronary arteries during intrauterine life.
Methods or Approach:
Studies were conducted on 50 autopsied infants who died during the first month of life for whom data were available on the smoking habits of mothers. The areas of arterial layers were measured with a planimeter from the photograph of arterial cross section.
Results to Date:
The intimal layers of the coronary arteries of infants whose mothers smoked during pregnancy were smaller than those of infants of nonsmoking mothers. The difference was independent of sex, birth weight, heart weight, and infection. Tobacco smoking appears to prevent normal development of the intimal layer of fetal coronary arteries. This retarded intrauterine development of the intima in infants of smoking mothers cannot be considered a preatherosclerotic change.
Project Dates:
January 1983–December 1983.
Reference:
Lehtovirta, P.; Pesonen, E.; Sarna, S. "Effect of Smoking on the Fetal Coronary Arteries." *Acta Pathologica, Microbiologica et Immunologica Scandinavica, Section A,* 92:189-193, 1984.

0194. INSTITUTE OF OCCUPATIONAL HEALTH, Haartmaninkatu 1, SF-00290 Helsinki, Finland.

Project Title:
Biological Monitoring of Active and Passive Exposure to Tobacco Smoke.

Principal Investigators:
Sorsa, M.; Husgafvel-Pursiainen, K.; Einisto, P., et al.
Objective:
To compare exposure of passive and active smokers in relation to exposure to various types of smoke components.
Methods or Approach:
While active smokers show increased frequencies of sister chromatid exchanges and chromosome aberrations in peripheral blood lymphocytes, and exhibit mutagenicity in urine, very little is known about exposure of passive smokers to environmental tobacco smoke. Groups of well-defined passive smokers exposed to smoke occupationally or at home are compared with active smokers for such chromosomal damage and urine mutagenicity, and for more conventional biological smoking measures (i.e., thiocyanates, thioethers, carboxyhemoglobin (COHb), and nicotine/cotinine). All biological exposure measures are correlated with data on environmental monitoring and long-term smoke exposure by personal interviews and questionnaires.
Results to Date:
Preliminary data on active smokers showed no short-term differences between low-tar and medium-tar cigarette smokers in COHb, thioethers, or urinary mutagenicity. However, after sitting in the same exposure chamber, active smokers differed significantly from passive smokers in COHb and plasma cotinine. Plasma thiocyanates were poor indicators for short-term exposure. Urinary mutagenicity values in passive smokers were higher than in nonsmokers, and only slightly lower than among active smokers.
Project Dates:
January 1980–December 1986.
Financial Support:
National Board of Health, Finland (SA 030/64).

0195. INSTITUTE OF OCCUPATIONAL HEALTH, Haartmaninkatu 1, SF-00290 Helsinki, Finland.

Project Title:
Mutagenicity of Cigarette Smoke Condensates (CSCs) and Environmental Tobacco Smoke Samples.

Principal Investigators:
Sorsa, M.; Husgafvel-Pursiainen, K.; Salomaa, S., et al.
Objective:
To correlate mutagenic potencies of CSCs from different types and brands of cigarettes in relation to environmental smoke from tobacco smoking and wood burning, with special emphasis on environmental cigarette smoke in offices and restaurants.
Methods or Approach:
Different short-term tests for mutagenicity are being applied to study genotoxic potencies of complex tobacco-derived samples. Some samples are being correlated with chemical analyses of typical PACs. Both particulate and vapor phase are collected in environmental smoke samples.
Results to Date:
All CDCs are highly genotoxic in bacterial assays, in inducing sister chromatid exchanges (SCEs) in human lymphocytes, and in Chinese hamster ovary cells in vitro in a dose-related manner, and also without an exogenous metabolic system. SEC-inducing potency is similar in CSCs from American and Chinese brands of cigarettes; however, in relation to amount of condensate in the test system, CSCs from low-tar cigarettes are more efficient inducers of SCEs than the same amount of CSC prepared from medium- or high-tar cigarettes. Preliminary data show that environmental tobacco smoke (particulate phase, collected on filters) is highly mutagenic.
Project Dates:
January 1981–December 1986.
Financial Support:
National Board of Health, Finland.

0196. INSTITUTE OF OCCUPATIONAL HEALTH, Department of Industrial Hygiene and Toxicology, Haartmaninkatu 1, SF-00290 Helsinki 29, Finland.

Project Title:
Sister Chromatid Exchanges Among Workers Occupationally Exposed to Phenoxy Acid Herbicides 2,4-D and MCPA.

Principal Investigator:
Linnainmaa, K.
Objective:
To analyze frequencies of sister chromatid exchanges (SCEs) in workers using 2,4-dichlorophenoxyacetic acid (2,4-D) and 4-chloro-2-methylphenoxyacetic acid (MCPA) for foliage spraying in forestry; elucidate possible exposure-related changes in frequencies of SCEs.
Methods or Approach:
Before the spraying season, subjects underwent a physical examination that included an interview about occupational history, health status, and personal smoking and drinking habits. Only 50 persons considered healthy were accepted; 15 persons not working with herbicides served as controls. Three blood samples were taken from exposed workers: before the spraying period (at time of physical examination), in the

middle of the spraying period (6 to 36 days of exposure), and 2 days after spraying was completed. A urine sample was also taken with the second blood sample, to determine concentrations of 2,4-D and MCPA. Enough cells for SCE analysis were obtained from 35 workers and 15 controls.

Results to Date:
Concentrations of 2,4-D and MCPA in urine samples varied from 0.00 to 10.99 mg/L. No significant differences in frequencies of SCEs were observed in samples taken before, during, or after exposure. In addition, means of SCEs in nonexposed controls fell in the same range as those in exposed subjects. However, a difference in the means of SCEs was observed between smokers and nonsmokers, with smokers having significantly higher mean values than nonsmokers. Results support earlier data indicating that 2,4-D and MCPA do not act as direct DNA-damaging agents.

Financial Support:
Academy of Finland.

Reference:
Linnainmaa, K. "Sister Chromatid Exchanges Among Workers Occupationally Exposed to Phenoxy Acid Herbicides 2,4-D and MCPA." *Teratogenesis, Carcinogenesis, and Mutagenesis* 3:269-279, 1983.

0197. NATIONAL PUBLIC HEALTH INSTITUTE, Mannerheimintie 166, 00280 Helsinki, Finland.

Project Title:
North Karelia Project.

Principal Investigators:
Puska, P.; Tuomilehto, J.; Nissinen, A., et al.

Objective:
To implement and evaluate a comprehensive community-based intervention program in the county of North Karelia in eastern Finland.

Methods or Approach:
A comprehensive community-based intervention is carried out in the county (which has 180,000 inhabitants), to reduce coronary heart disease (CHD) and stroke rates through reduction of the population levels of established risk factors: smoking, elevated serum cholesterol, and elevated blood pressure. A matched reference area is used for evaluation. Large, cross-sectional representative population samples were examined in 1972 and after 5 years (1977) and 10 years (1982). Mortality data and information on other diseases were also collected for the two areas and the whole country.

Results to Date:
During the initial 5-year period, there was a net reduction in smoking in middle-aged males and females of 14 and 8 percent, respectively; there was also a reduction in other risk factors. Cardiovascular morbidity and mortality rates started to decline also. At 10-year followup, there was a net reduction in smoking of 28 percent in men and 14 percent in women. Serum cholesterol and systolic blood pressure both declined by 3 percent in men. Between 1974 and 1979, the age-standardized CHD mortality of males aged 35 to 64 years declined 22 percent in North Karelia, 12 percent in the reference area, and 11 percent in the whole country, excluding North Karelia. A prospective followup study of the original population sample has shown the strong independent role of smoking as a predictor of CHD or death in general.

Future Plans:
The intervention program will continue and a more integrated approach including several major noncommunicable diseases will be implemented. Followup will continue through 1992.

Project Dates:
January 1982–December 1994.

Financial Support:
National Public Health Institute; Finnish Government.

0198. NATIONAL PUBLIC HEALTH INSTITUTE, Department of Epidemiology, Mannerheimintie 166, 00280 Helsinki 28, Finland.

Project Title:
Finnish "Keys to Health" Program.

Principal Investigators:
Puska, P.; Koskela, K.; Wiio, J., et al.

Objective:
To conduct a large-scale field study of health behavior change in Finland.

Methods or Approach:
A 15-part television series, which modeled skills for smoking cessation, weight loss, dietary change, and physical activity, was broadcast. In one region of Finland, social reinforcement for those behaviors was organized by recruiting and training volunteers from each local community. Surveys of that region and a comparable neighboring area were conducted at baseline and during the program to assess program participation and effects. A random population survey was conducted in both areas before the program series began. Each person completing the questionnaire returned it to a municipal health center, at which time it was reviewed and the person was given a physical examination. Response rate was approximately 80 percent. Questionnaires contained items measuring sociodemographic variables, health status, physical activity, smoking habits, dietary habits, and psychosocial variables. The physical examination included height, weight, blood pressure, serum cholesterol, and serum thiocyanate. Surveys were conducted as part of a WHO-coordinated project independent of the "Keys to Health" series, and involved a random sample of about 8,000 inhabitants aged 25 to 64 years. A smaller cluster sample in municipal zones was used to provide a baseline sample for studying program effects. A followup postal survey was mailed to respondents to baseline sample before the last of the weekly broadcasts. Responses were intended to represent involvement with, perceptions of, and short-term results associated with the television series and related activities. More than 80 percent of the sample responded to the second survey. From followup respondents, 12 successful smoking quitters, 12 successful weight losers, and 12 controls were selected for further study. After approximately 6 months, the 36 individuals participated in face-to-face interviews where persistence of change was measured, factors contributing to achievements were observed and discussed, and body weight, serum cholesterol, and serum thiocyanate were measured.

Results to Date:
Short-term behavior changes were similar in both regions, but more persons reported sustained smoking cessation and loss of >5 kg body weight in the region where the supportive community program was organized.

Future Plans:
Similar activities will continue.

Project Dates:
January 1982–continuing.

Financial Support:
National Public Health Institute, Finland.

0199. NATIONAL PUBLIC HEALTH INSTITUTE, Unit of Statistics, Kalliolinnantie 4, SF-00140 Helsinki, Finland.

Project Title:
Economic Aspects of Smoking.

Principal Investigator:
Pekurinen, M.
Objective:
To develop a policy-relevant economic simulation model for analyzing effectiveness and efficiency of alternative policy options aimed at reducing smoking.
Methods or Approach:
Econometric methods are used to model demand for tobacco products (separately for cigarettes, pipe tobacco, and cigars). Health and economic costs are quantified by standard epidemiologic and multivariate methods, utilizing official statistics and survey data collected by the National Insurance Institution. Future incidence of the main smoking-related diseases will be predicted by an econometric model that relates disease incidence to cigarette price, income, and health education. Inflation and tax revenue effects of alternative smoking reduction strategies will be modeled by methods used by the Ministry of Finance.
Results to Date:
Cigarette prices appear to be the main determinant of demand in Finland. Price elasticity of cigarettes is about -.95 to falling real prices and -.5 to rising real prices. Income elasticity is about +.5. Demand for pipe tobacco is mainly determined by cigarette prices; cross-price elasticity is about +2.00, and own price elasticity is about -0.6. Health education appears to have permanently reduced demand for cigarettes by 6 percent since 1976. Conservative estimates of annual smoking-related health losses amount to 2,800 premature deaths, 800 persons permanently disabled, and 170,000 working days lost to sickness absence. Patients with smoking-related disease occupy 760 beds in general hospitals throughout the year. Minimum estimate of the economic cost of smoking in Finland is 1,560 million Fmk/year.
Future Plans:
Data analysis will continue and submodels will be linked together.
Project Dates:
January 1984–December 1985.
Financial Support:
National Board of Health, Finland.

0200. NATIONAL PUBLIC HEALTH INSTITUTE, Mannerheimintie 166, 00280 Helsinki 28, Finland.

Project Title:
The North Karelia Youth Project.

Principal Investigators:
Vartiainen, E.; Pallonen, U.; Puska, P.
Objective:
To test the feasibility and effects of a large-scale health education program among 12- to 16-year-old schoolchildren.
Methods or Approach:
The North Karelia Youth Project is based on results of pilot studies and forms part of the Finnish National Public Health Institute's more general goal, the development and demonstration of methods for primary prevention of noncommunicable diseases and health promotion. More specific aims are to prevent cigarette smoking and improve nutrition (decrease total fat in diet, increase proportion of polyunsaturated fats, and decrease salt and sugar consumption). The 24 schools in North Karelia and 16 randomly selected schools in the County of Kuopio are randomly assigned to five different intervention groups. In group 1, direct intervention will be carried out by project workers, teachers, and trained peer leaders. In group 2, intervention will be conducted mainly by teachers, with training and assistance by health educators of the project. In North Karelia, the group 2 program will be largely administrative, providing recommendations and supplying written and audiovisual material to all schools. Experiences from this group are essential for planning national applications. To compare the possible effect of the North Karelia project, the program is organized also in the reference county in eight schools in exactly the same way as the teacher-led schools in North Karelia. Eight schools in the County of Kuopio are control schools.
Results to Date:
Data from a pilot study in North Karelia (1978-1980) indicate that one-third of the onset of smoking could be prevented by using the methods. The main aim of the program was to teach children the skills necessary to resist social pressures to start smoking. In another pilot study, it was noticed that the extremely high serum cholesterol level (mean approximately 5 mmol/L) among Finnish children could be decreased about 15 percent by dietary changes.
Future Plans:
If results are positive, the program may be receive nationwide implementation.
Project Dates:
January 1984–December 1988.
Financial Support:
National Board of Health, Finland; The Academy of Finland; State's Alcohol Monopoly Company, Finland.

0201. NATIONAL PUBLIC HEALTH INSTITUTE, FINLAND, Mannerheimintie 166, 00280 Helsinki 28, Finland.

Project Title:
Monitoring of Smoking and Other Health Related Lifestyles in Finland.

Principal Investigators:
Puska, P.; Piha, T.; Niemensivu, H.
Objective:
To monitor national smoking rates and other health-related lifestyles in the Finnish adult population by annual surveys; evaluate national health education programs and relate lifestyle changes to changes in disease rates.
Methods or Approach:
Annual followup (since 1978) has been carried out by mail surveys of independent cross-sectional random samples of the Finnish population aged 15 to 64 years. Each year the sample size is between 5,000 and 6,000. An additional sample (approximately 1,200) from the County of North Karelia is also surveyed to monitor trends in this area with special community-based interventions (North Karelia project). Response rates are around 80 percent. Standard questions (unchanged) on smoking and other lifestyle factors have been repeated annually. Special questions have been added each year to evaluate special health education programs, especially the national smoking cessation and behavior modification television programs of the North Karelia project.
Results to Date:
National trends in smoking in Finland from 1978 to 1984 have been published. Smoking among men decreased from 39 percent to 36 percent, and among women from 20 percent to 19 percent. Smoking declined more rapidly in North Karelia

than in the rest of the country; in men from 42 percent in 1978 to 38 percent in 1984, and in women from 18 percent to 15 percent. Trends are associated with reduction of coronary mortality in Finland as a whole, and with an even greater reduction in North Karelia. Surveys have also indicated that the national television programs have had favorable effects and have clearly been cost-effective measures.

Future Plans:
Monitoring will continue on an annual basis. Trends will also be related to national trends of major noncommunicable diseases, especially cardiovascular disease and cancer.

Project Dates:
January 1978–continuing.

Financial Support:
National Board of Health, Finland.

0202. SALO DISTRICT HOSPITAL, Salo, Finland 24130.

Project Title:
Effects of Maternal Smoking on Fetal Heart Rate Variability and Cord Gas Values During Pregnancy and Labor in Unselected Material.

Principal Investigators:
Kariniemi, V.; Rosti, J.

Objective:
To determine whether maternal smoking has chronic effects on fetal heart rate variability, which reflects the integrity of the fetal autonomous nervous system.

Methods or Approach:
The approximately 600 mothers who deliver each year at the Salo District Hospital represent an unselected population, and 99 percent regularly visit the outpatient clinic for monthly checkup of hemoglobin, blood pressure, weight, and urine protein and glucose levels. Ultrasound examination is made during the midtrimester of pregnancy and antepartal analysis of FHR variability during the 2 to 3 weeks before delivery. All fetuses that go to labor are monitored for FHR variability throughout labor and delivery. A sample of venous cord blood is drawn for gas analysis. Data is stored on a computer for further analysis. A 5-minute sample of abdominal fetal electrocardiogram and 10-minute samples of abdominal or direct fetal electrocardiograms are used for antepartal and intrapartal analysis of FHR variability.

Results to Date:
Fifteen percent of mothers admit smoking at least one cigarette/day during pregnancy. Fetuses of mothers who smoke show a higher differential index of the fetal electrocardiogram (beat-to-beat variability) during the first stage of labor than those of nonsmoking mothers. The partial pressure of carbon dioxide in the cord vein of mothers who smoke is also higher than that of the nonsmoking group.

Future Plans:
More material will be collected for the evaluation of antepartal FHR variability of smokers vs. nonsmokers, and alcohol use by mothers will be determined to study the combined effects of smoking and alcohol consumption.

Project Dates:
January 1983–continuing.

Financial Support:
Salo District Hospital; The Paulo Foundation.

Reference:
Kariniemi, V.; Rosti, J. "Fetuses of Smoking Mothers Have Higher Heart Rate Variability and Cord Vein Carbon Dioxide Than Controls During Labor," submitted for publication.

0203. UNIVERSITY OF HELSINKI, Department of Public Health Science, Kalliolinnantie 4, 00140 Helsinki, Finland.

Project Title:
The Finnish Twin Cohort Study.

Principal Investigators:
Koskenvuo, M.; Kaprio, J.; Langinvainio, H., et al.

Objective:
To study interactions of genetic and enviromental factors in the etiology of chronic disease.

Methods or Approach:
All adult like-sexed twin pairs in Finland (> 17,000 pairs) born before 1958 and alive in 1967 form the base population. Two health questionnaires were sent to all twins in 1975 (response rate 89 percent) and in 1981 (response rate 84 percent) in addition to small subsample studies. Morbidity followup is from death certificates, hospital admissions, the Finnish Cancer Registry, and other medical registries.

Results to Date:
In male pairs discordant for smoking and free of coronary heart disease (CHD) at baseline, incidence of CHD and total mortality was significantly higher among smoking cotwins than among nonsmoking cotwins during 6 years of followup. Other results have been published.

Future Plans:
Followup of the cohort will continue.

Project Dates:
1974–continuing.

Financial Support:
University of Helsinki, Finland; NCI (5R01CA32262-03); MRC, Finland; CTR.

0204. UNIVERSITY OF KUOPIO, P.O. Box 6, 70211 Kuopio 21, Finland.

Project Title:
Kuopio Ischaemic Heart Disease Risk Factor Study (KIHD).

Principal Investigators:
Salonen, J.T.; Rauramaa, R.; Huttunen, J.K., et al.

Objective:
To investigate the impact and interactions of the course of life, physical activity, diet, smoking, social activity and support, and personality on risk of ischemic heart disease (IHD) and on progression of atherosclerosis; determine underlying biological mechanisms.

Methods or Approach:
The study design comprises a prospective followup of cohorts based on total population samples of all eligible men (aged 54 and 45 at entry). Approximately 2,000 and 1,200 participants are expected in baseline examination of the two age strata, respectively. The target population lives in the city of Kuopio and in eight surrounding communities in eastern Finland, the area with the highest recorded mortality from IHD and incidence of myocardial infarction (MI). Baseline examinations will take place between March 1984 and June 1988. Three-year reexaminations will be carried out during 1988 and 1991. Measurement instruments include interview and self-administered questionnaires, 4-day supervised food recording, maximal exercise test with computerized ECG and respiratory gas analysis, 24-hour Holter-type monitoring, ultrasonographic measurements of arterial wall thickness, lumen diameter, and flow disturbances of femoral and carotid arteries, and a comprehensive set of chemical and hematological tests on blood, urine, and adipose tissue samples.

Results to Date:
Participation rate in baseline examinations is approximately 80 percent of 600 subjects who received invitations to participate. Preliminary findings show high prevalence of various manifestations of IHD, hypertension, and mild left ventricular dysfunction. Validity of self-reported smoking appears very high as assessed by determinations of cotinine and thiocyanate in serum.
Future Plans:
The study will test the hypothesis that smoking elevates the risk of IHD through increasing aggregation tendency of thrombocytes and, to a lesser extent, through promoting progression of arterial atherosclerosis due to changes in lipoprotein and catecholamine metabolism.
Project Dates:
January 1983–December 1992.
Financial Support:
Finnish Academy; Finnish Medical Board; Finnish Council for Exercise Sciences; University of Kuopio.

0205. UNIVERSITY OF KUOPIO, Department of Community Health, P.O. Box 6, 70211 Kuopio, Finland.

Project Title:
Health in Finnish Village.

Principal Investigators:
Kupusalo, E.; Neittaanmaki, L.; Lappi, T., et al.
Objective:
To clarify health behavior of populations in static, negative, and positive growth phase villages according to self-identity and sources of adopted health information; determine effects of official programmed intervention and an intervention occurring through villagers' initiative to promote health.
Methods or Approach:
Health behavior characteristics studied include nutrition, alcohol consumption, smoking, and physical fitness. Populations will be interviewed and clinical examinations will be conducted, supported by certain blood tests such as cotinine determination for smoking status. Health care personnel in one village will be trained to provide up-to-date information on nutrition and exercise. Research personnel will collaborate with the village council.
Results to Date:
Project is in a preliminary phase.
Project Dates:
1985–1988.
Financial Support:
National Board of Health, Finland.

0206. UNIVERSITY OF OULU, Department of Physiology, Kajaanintie 52 A, SF-90219 Oulu 22, Finland.

Project Title:
Combined Effects of Smoking and Reduction of Oxygen Pressure on Physical Performance.

Principal Investigators:
Hirvonen, L.; Forsberg, S.
Objective:
To assess the influence of smoking on athletic endurance performance under reduced atmospheric pressure.
Methods or Approach:
Ergometer tests were conducted under normal atmospheric pressure and in a low-pressure chamber with and without previous smoking. The test subjects ($n = 19$) were young male members of a football club. Heart rate was measured by continuous ECG recording. Blood carbon monoxide content was 3 to 4 percent after two cigarettes. Physical working capacity was measured on the basis of three successive 4-minute loading periods. Maximum oxygen uptake was estimated according to von Dobeln. The chamber pressure was decreased to correspond to an altitude of 3,000 m ($PO_2 = 14\text{-}15$ kPa).
Results to Date:
Hematological, cardiovascular, and lung function status of the test subjects were normal. Smoking decreased the maximum oxygen uptake under normal atmospheric pressure from the average of 3.58 L/min to 3.38 L/min (5.6 percent). Under low pressure it decreased further to 2.84 L/min (20.7 percent lower than initially). The maximum oxygen uptake of the nonsmokers decreased from the initial value of 3.57 L/min to 3.07 L/min (14.8 percent less under low pressure than initially). All the above- mentioned changes were significant ($p < 0.005$). The effects of smoking and decrease of atmospheric oxygen pressure appear to be cumulative. The experimental part of the study has been completed and a report is being prepared.
Project Dates:
October 1981–1982.
Financial Support:
Juho Vainio Foundation; University of Oulu.

0207. UNIVERSITY OF OULU, Department of Physiology, Kajaanintie 52 A, SF-90219 Oulu 22, Finland.

Project Title:
Premises and Results of Smoking Withdrawal.

Principal Investigator:
Hirvonen, L.
Objective:
To map the interest in smoking cessation; estimate the results of withdrawal therapy.
Methods or Approach:
Willingness to stop smoking was estimated by questionnaires in selected population groups. The number of participants in cessation clinics was compared with the local population. The success rate of 1,700 participants in 17 cessation clinics (5-Day Plan) held in various parts of Finland in 1973 through 1980 was collected by questionnaire 12 months retrospectively.
Results to Date:
A total of 10,500 questionnaires were distributed to the staff members of Oulu University Hospital and Oulu University staff and university students. Of the 83 percent who responded, 25.3 percent of the men and 20.3 percent of the women smoked. Willingness to stop was expressed by 68 percent of male ($n = 1,122$) and 78 percent of female ($n = 839$) smokers; 89 percent of the men and 79 percent of the women who wanted to quit preferred to try doing so on their own. Therapy in a small group was desired by 9 percent and in a large group by 3 percent. There were 1,085 ex-smokers among the university staff and students, representing 17.4 percent of the total number and 22.6 percent of the nonsmokers. Two-thirds had stopped smoking more than 2 years previously. When a smoking withdrawal clinic was initiated for the hospital staff ($n = 2,800$), four smokers registered. A fresh attempt resulted in two people registering. After a regular newspaper advertisement (two to three times) 0.1 to 1.0 percent of the population in a community are usually participating in a 5-day withdrawal program. A series of 1,700 participants in 17 different 5-day plan withdrawal courses will be analyzed and the results correlated with personal data, smoking history, some test results, withdrawal symptoms, observation of instruction and methods of instruction, and criticism by participants of the withdrawal activity.

Project Dates:
1973–1983.
Financial Support:
Juho Vainio Foundation; University of Oulu.
Reference:
Hirvonen, L. "Smoking Cessation by The Five-Day Plan in Finland." *Acta University Oulo* D123, Medical Publication 4, 1984, 180 pp.

0208. UNIVERSITY OF OULU, Departments of Physiology and Public Health Sciences, Kajaanintie 52 A, SF-90219 Oulu 22, Finland.

Projcet Title:
Smoking Habits of the University Staff and Students.

Principal Investigators:
Hirvonen, L.; Kari-Koskinen, O.
Objective:
To obtain information about the smoking habits among the Oulu University staff and students, changes in their habits, and their plans to reduce smoking.
Methods or Approach:
The data from the survey questionnaire, returned by 88 percent of the 1,600-member staff and 78 percent of the 6,200 students, were computerized for analysis.
Results to Date:
Among the staff 76.3 percent of the males and 80.9 percent of the females were nonsmokers. The corresponding percentages for the students were 74.6 and 79.8. Two-thirds of the smokers smoked daily. The frequency of smokers by faculty varied among the male staff from 15 percent (sciences) to 44 percent (humanities); among the females from 16 percent (education) to 20 percent (medicine and technology). The corresponding percentages of the male students were 20 (medicine) to 36 (humanities), and of the female students 16 (sciences) to 26 (humanities). Also, 25 percent of the staff members and 15 percent of the students were ex-smokers; 80 percent of the staff ex-smokers and 62 percent of the student ex-smokers had stopped more than 2 years previously. Although smoking was regarded as harmful to health by 95 percent of the total series, 20-30 percent of the regular smokers and 17-53 percent of the occasional smokers responded that they did not want to stop. Smoking has decreased 40-50 percent since the 1960s among male students, but has remained unchanged among the females. Results will be submitted for publication.
Project Dates:
August 1980–1982.
Financial Support:
Juho Vainio Foundation; University of Oulu.

0209. UNIVERSITY OF OULU, Department of Physiology, Kajaanintie 52 A, SF-90220 Oulu, Finland.

Project Title:
Reasons for Interrupting Smoking Cessation.

Principal Investigator:
Hirvonen, L.
Objective:
To elucidate reasons for withdrawal from cessation of smoking program.
Methods or Approach:
About 30 percent of people participating in the Five-Day Plan to Stop Smoking courses interrupt for various reasons. Good immediate and long-term prognosis is predicted by regular participation in course sessions. Questionnaires are mailed to participants with special emphasis on reasons for not continuing in the program to determine differences between interrupters and participants who attend regularly.
Results to Date:
Preliminary analysis indicates the most frequent reasons for not continuing are disproportion of the course program and expectations directed at it, severe withdrawal symptoms, and weakness of motivation to quit smoking.
Project Dates:
January 1984–1986.
Financial Support:
University of Oulu; Central Medical Board (Finland).

0210. UNIVERSITY OF OULU, Department of Physiology, Kajaanintie 52 A, SF-90220 Oulu, Finland.

Project Title:
Effect of Nicotine on Myocardiac Functions.

Principal Investigators:
Hirvonen, L.; Kettunen, R.; Timisjarvi, J.
Objective:
To analyze the influence of nicotine on in vivo changes in the heart under various conditions.
Methods or Approach:
Catheter tip manometers are introduced into both ventricles, aorta, and pulmonary artery for pressure recordings. Ventricular volumes and cardiac output are recorded by thermodilution method. Recordings of both sides are made simultaneously. Signal processing and computing are done on-line. Numerous parameters are recorded and calculated in various phases of the cardiac cycle. Laboratory-bred beagle dogs are used as experimental animals. Special attention is paid to excitation-contraction coupling.
Results to Date:
Project is in a preliminary phase, but previous studies have shown that nicotine impairs physical performance by increasing heart rate and cardiac work, increasing pulmonary capillary pressure and speed of ventricular pressure rise, and decreasing ventricular residual volume. Effects can be inhibited by beta-adrenergic blockade.
Future Plans:
Experiments with myocardial cell preparations are planned.
Project Dates:
March 1985–1986.
Financial Support:
Juho Vainio Foundation, Finland; University of Oulu.

0211. UNIVERSITY OF OULU, Department of Pharmacology, Kajaanintie 52 D, SF-90220 Oulu, Finland.

Project Title:
Cigarette Smoking and Human Placental Xenobiotic and Steroid Metabolism.

Principal Investigators:
Pelkonen, O.; Pasanen, M.; Vahakangas, K.
Objective:
To study the effect of cigarette smoking on placental metabolism of steroids and foreign chemicals; determine possible relationships between chemicals and steroids.
Methods or Approach:
Placental subcellular preparations (microsomes, mitochondria) are incubated in vitro to study biotransformations of different steroids (aromatase activity, cholesterol side-chain cleavage activity) and xenobiotics (aryl hydrocarbon hydroxylase, 7-ethoxycoumarin O-deethylase, and 7-ethoxyresorufin O-deethylase). Cigarette smoke exposure is measured by plasma cotinine.

Results to Date:
Methods for measuring different steroid biotransformations and for purification of placental oxidative enzymes (cytochromes P-450) have been developed. Survey of effects of cigarette smoking on different aspects of placental biotransformations is continuing.
Future Plans:
Placental markers for the effects of cigarette smoking will be identified and used in future epidemiological studies.
Project Dates:
January 1982–continuing.
Financial Support:
University of Oulu.

0212. UNIVERSITY OF OULU, Departments of Pharmacology and Anatomy, SF-90220 Oulu 22, Finland.

Project Title:
Transplacental Toxic Effects of Cigarette Smoke in Mice and the Genetically Controlled Responsiveness to Polycyclic Aromatic Hydrocarbons.

Principal Investigators:
Vahakangas, K.; Rajaniemi, H.; Pelkonen, O.
Objective:
To evaluate role of genetically controlled responsiveness to polycyclic aromatic hydrocarbons (PAH) in effects of cigarette smoke on birth weight and on possible transplacental toxic effects on ovaries.
Methods or Approach:
Pregnant PAH-responsive C57BL/6 and PAH-nonresponsive DBA/2 mice are treated with cigarette smoke from days 1 to 18 of pregnancy. Fetal size and aryl hydrocarbon hydroxylase in various tissues are measured. Ovarian histology in mothers and offspring is studied.
Results to Date:
Genetically determined responsiveness to PAH was not found to be important in effect of cigarette smoke on birth weight or ovarial histology. Judged by the number, primordial oocytes during fetal life seemed to be more sensitive to components of cigarette smoke than in adulthood.
Project Dates:
1980–1985.
Financial Support:
University of Oulu, Finland; Finnish Cancer Research Foundation.

0213. UNIVERSITY OF TAMPERE, INSTITUTE OF CLINICAL SCIENCES, Teiskontie 35, 33 520 Tampere, Finland.

Project Title:
Smoking and Pregnancy.

Principal Investigators:
Pulkkinen, P.; Tuimala, R.
Objective:
To evaluate effects of maternal smoking on outcome of pregnancy and on the newborn; study balance between mother newborn, and placenta of some trace elements (cadmium, selenium, chromium, copper, zinc, magnesium).
Methods or Approach:
The prospective study of 40 pregnant smokers and 40 matched nonsmokers included monthly ultrasound examination to follow fetal biparietal and antero-posterior body cross-section growth. Maternal smoking was verified by testing for thiocyanate in maternal serum during each trimester and in cord blood of neonate. Thiocyanate was measured by colorimetric method, selenium by spectrofluorometry, and other trace elements by atomic absorption spectrometry.
Results to Date:
Growth retardation in fetuses of smokers was visible by ultrasonic examination at 16 weeks. Lower weight in neonates of smokers was independent of any other factor. Levels of serum thiocyanate (apparently a good indicator of smoking) were similar in maternal and cord blood, indicating a free passage of thiocyanate from mother to fetus. All trace elements have not been measured at this time.
Future Plans:
October 1981–December 1985.
Project Dates:
University of Tampere, Finland.

0214. UNIVERSITY OF TURKU, Department of Physiology, Kiinamyllynkatu 10, SF-20520 Turku, Finland.

Project Title:
Effect of Cigarette Smoke on the Pulmonary Metabolism of Arachidonic Acid.

Principal Investigators:
Mannisto, J.; Uotila, P.
Objective:
To investigate effect of cigarette smoke on incorporation of arachidonic acid into pulmonary phospholipids and on pulmonary metabolism of arachidonic acid into prostaglandins and related compounds.
Methods or Approach:
The effect of cigarette smoke on the fate of exogenous arachidonic acid was investigated in isolated perfused rat and hamster lungs. ^{14}C-arachidonic acid was infused into the pulmonary circulation, and distribution of radiolabel in pulmonary lipids and amount of arachidonate metabolites in perfusion effluent were analyzed.
Results to Date:
Pre-exposure of animals to cigarette smoke daily for 3 weeks did not change amounts of metabolites in lung effluent or incorporation of arachidonic acid into lung lipids. Cigarette smoke ventilation of lungs from pre-exposed hamsters changed amounts of some metabolites in the effluent. Cigarette smoke ventilation increased the amount of ^{14}C-arachidonic acid in the triacylglycerols of the perfused rat and hamster lungs, but had no clear effect on amount of radioactivity in diacylglycerols or different phospholipids. The increased amount of radiolabel in triacylglycerols was significantly greater in hamster lungs ventilated with smoke from medium- or high-tar cigarettes than in those ventilated with low-tar cigarette smoke.
Project Dates:
1977–1984.
Financial Support:
University of Turku, Finland; NIEHS (ES-01684).

0215. UNIVERSITY OF OULU, Department of Pharmacology, SF-90219 Oulu 22, Finland. DHHS, NIH, NCI, Laboratory of Molecular Carcinogenesis, Bethesda, Maryland 20205.

Project Title:
Effects of Smoking on Human Drug Metabolism and Measures for Smoking.

Principal Investigators:
Vahakangas, K.; Pelkonen, O.; Sotaniemi, E.A.
Objective:
To study effects of smoking on parameters of human drug

metabolism; investigate the possibility of determining smoking status objectively.

Methods or Approach:

In vitro parameters (aryl hydrocarbon hydroxylase (AHH), 7-ethoxyresorufin O-deethylase (ERDE), cytochrome P-450 and others) from liver biopsy samples, and in vivo parameters (antipyrine clearance and antipyrine half-life) of drug metabolism are used. Various parameters (serum and urine thiocyanate, urine nicotine and cotinine, blood carbon monoxide, urine thioether concentrations) for smoking status are studied to determine the best possible combination to be used in clinical studies.

Results to Date:

AHH and cytochrome P-450 were not induced by cigarette smoking. Antipyrine clearance was increased, however, and antipyrine half-life shortened in smokers. Thiocyanate concentration in serum alone seems to be a good, although not absolute, qualitative measure for smoking. Plasma cotinine seems to be a better index for smoking. Liver ERDE activity is clearly associated with cigarette smoking. Monoclonal antibody against AHH-induced rat hepatic cytochrome P-450 inhibits human liver ERDE activity, indicating the analogous nature of human and rat enzymes.

Project Dates:

1979–continuing.

Financial Support:

University of Oulu.

0216. UNIVERSITY OF OULU, Department of Pharmacology, SF-90220, Oulu 22, Finland. DHHS, NIH, NCI, Laboratory of Human Carcinogenesis, Bethesda, Maryland 20205.

Project Title:

Benzo(*a*)pyrene Metabolism and DNA-Binding in the Placenta.

Principal Investigators:

Vahakangas, K.; Pasanen, M.; Trivers, G., et al.

Objective:

To study placental barrier/activation system for xenobiotics using benzo(*a*)pyrene (BaP) as a model chemical.

Methods or Approach:

BaP-DNA adducts in placentas from both smoking and nonsmoking mothers are studied by synchronous fluorescence spectrophotometry (SFS) and ultrasensitive enzymatic radioimmunoassay (USERIA).

Results to Date:

Adducts have been detected in human placentas by both SFS and USERIA.

Project Dates:

1983–continuing.

Financial Support:

University of Oulu, Finland.

FRANCE

0217. ECOLE NATIONALE SUPERIEURE DE CHIMIE, 3, Rue Alfred Werner, 68011 Mulhouse Cedex, France. P.O. BOX 1951, 4001 Basle 1, Switzerland.

Project Title:

Determination of Nicotine in Allergenic Extracts of Tobacco Leaf by High Performance Liquid Chromatography.

Principal Investigators:

Sudan, B.J.L.; Strehler, C.; Strub, H., et al.

Objective:

To (1) determine nicotine content of allergenic extracts of tobacco leaf; (2) detect cotinine (photodegradation product of nicotine) in such extracts; (3) control standardization of allergenic extracts of tobacco leaf in an international program by high performance liquid chromatography (HPLC); and (4) obtain better results in specific desensitization of patients allergic to nicotine as a hapten.

Methods or Approach:

Eight allergenic extracts of tobacco leaf were investigated by HPLC to determine levels of nicotine and cotine. Allergenic extracts were prepared using extraction, maceration time, method of sterilization, and membrane filtration to study nicotine content variability.

Results to Date:

Good separations of nicotine and cotinine contents of allergenic extracts were achieved using HPLC. Nicotine content was also dependent on extraction method, maceration time, sterilization method, and membrane filtration. Analysis showed tobacco extracts had markedly different nicotine patterns. Cotinine was not detected. Specific desensitization with allergenic extracts of tobacco leaves is useful when using a freshly prepared allergen containing a threshold dose of nicotine in a case of familial dermatitis that resembles seborrhoeic dermatitis. Standardization of allergenic extracts is necessary to optimize results of specific desensitization after allergic skin tests to tobacco antigens in patients reacting to nicotine as a hapten.

Project Dates:

May 1983–April 1984.

Financial Support:

Ecole Nationale Superieure de Chimie.

Reference:

Sudan, B.J.L.; Brouillard, C.; Strehler, C., et al. "Determination of Nicotine in Allergenic Extracts of Tobacco Leaf by High Performance Liquid Chromatography." *Journal of Chromatography* 288:415-422, 1984.

0218. FACULTE DE MED PITIE-SALPETRIERE, Department of Biochemistry, 91 Boulevard de l'Hopital, 75634 Paris, Cedex 13, France.

Project Title:

Effects of Age, Pathology, Smoking, and Alcohol Addiction on

Different Biochemical Variables in a Large Unselected Elderly Population.

Principal Investigators:
Touitou, Y.; Proust, J.

Objective:
To determine effects of smoking, among other parameters, on plasma levels of carcinoembryonic antigen, ferritin, melatonin, plasma and erythrocyte calcium, magnesium, potassium, and enzymes; study the relationship of these factors to pathology and autopsy findings.

Methods or Approach:
Conventional biochemical determinations, using RIA and/or EIA methods, were made in an unselected population of elderly men and women (approximately 800). About one-third of the population was autopsied.

Results to Date:
A decrease of plasma levels of melatonin was found in current smokers, both male and female. There was apparently no effect on alkaline phosphatase levels, but an increase in levels of gamma-glutamyltranspeptidase was found.

Future Plans:
Data on cations, ferritin, and B_2 microglobulin will be analyzed.

Project Dates:
1983–1985.

Financial Support:
Faculte de Med Pitie-Salpetriere.

References:
(1) Touitou, Y., et al. "Age and Sex-Associated Modifications of Plasma Melatonin Concentration in Man. Relationship to Pathology, Malignant or Not, and Autopsy Findings." *Acta Endocrinologia (Kbh)* (In press). (2) Touitou, et al. "Biological and Pathological Factors Affecting Plasma GGT and Alkaline Phosphatase Activity in the Elderly." *Clinica Chimica Acta* (In press).

0219. HOPITAL HENRI MONDOR, Unite 139 de l'Inserm de Nephrologie, Cretcel, France.

Project Title:
Evaluation of Smoking Cessation Methods.

Principal Investigators:
Lagrue, G.; Geslin, P.; Grimaldi, B., et al.

Objective:
To develop a method for evaluating tobacco withdrawal programs.

Methods or Approach:
Relevant data were reviewed to establish evaluation protocol and treatment factors that must be included to provide reliable results.

Results to Date:
If a medication is used, a double-blind study is necessary. Healthy volunteers (smokers of >20 cigarettes/day for >5 years, not on medications, and without apparent psychological disturbances) should be randomly assigned to treatment or placebo group and personal factors should be determined. Success should be evaluated after 1, 3, 6, and 12 months, with subjects not answering questionnaires or telephone calls considered as treatment failures. Biological tests should be included (10 to 20 percent of smokers give false statements about quitting). Serum and saliva thiocyanate levels provide better indications of smoking status than nicotine in blood and urine, or carbon monoxide in expired air. Results must be evaluated statistically according to age, sex, social and cultural environment, and duration and intensity of smoking. Withdrawal symptoms such as weight gain and insomnia must also be considered. Study data have demonstrated a lack of difference between placebo and active medications. There are difficulties in using the double-blind approach and there is a question of psychological and physiological dependence. Motivation is of particular importance in successful treatment.

Financial Support:
INSERM.

Reference:
Lagrue, G. "Les Methodes de 'Desintoxication' Tabagique (Regles Generales Concernant Leur Etude)." [Methods of Tobacco 'Detoxication' (General Rules for Its Study)."] In: Molimard, R. (Editor). *2ème Journee de la Dependance Tabagique,* Comptes Rendus, U.E.R. Biomedicale des Saints-Peres, Paris, March 17, 1984, pp. 48-62, French.

0220. HOPITAL SALVATOR, LABORATOIRE D'EXPLORATIONS FONCTIONNELLES RESPIRATOIRES, 249 Boulevard de Ste-Marguerite, F 13374 Marseille, France.

Project Title:
Influence of Chronic Smoking on the Leukocytes.

Principal Investigators:
Vanuxem, D.; Sampol, J.; Grimaud, C.

Objective:
To investigate the influence of chronic smoking on leukocytes in smokers and nonsmokers.

Methods or Approach:
Total leukocyte count, neutrophil concentration, lymphocyte concentration, and carboxyhemoglobin concentrations were determined in 21 chronic smokers and 22 nonsmokers.

Results to Date:
There was a significant increase in total leukocyte count ($2p<0.001$), neutrophil concentration ($2p<0.001$), and lymphocyte concentration ($2p<0.01$) in smokers compared with nonsmokers. However, only total leukocyte count and neutrophil count proved to be correlated with carboxyhemoglobin saturation. It is hypothesized that carbon monoxide and/or carboxyhemoglobin act directly on peripheral blood leukocytes or indirectly (via adrenalin secretion). Average leukocyte count in smokers corresponds to the upper borderline count in nonsmokers; therefore, the number of cigarettes smoked/day should be taken into consideration when assessing a smoker's leukocytosis.

0221. INSERM UNIT 14, PHYSIOPATHOLOGIE RESPIRATOIRE, 54511 Vandoeuvre les Nancy, France.

Project Title:
A Longitudinal Study of Symptoms and Respiratory Function in Iron Miners.

Principal Investigators:
Pham, Q.T.; Mur, J.M.; Techlescu, D., et al.

Objective:
To conduct a resurvey of a cohort of iron miners examined 5 years previously to answer questions on reversibility of respiratory symptoms, incidence of bronchitis or asthma, and changes in pulmonary symptoms and pulmonary function tests according to cigarette smoking and/or hazards at the workplace.

Methods or Approach:
The original cohort consisted of 1,179 miners, randomly selected from 5,300 workers aged 35 to 55 (with normal x rays). Of those alive 5 years later, 871 were reexamined. The same examinations were performed: standard respiratory questionnaire with additional questions on work history, and

measurements of vital capacity (VC), forced expiratory volume in 1 sec (FEV_1), residual volume, and fractional uptake of carbon monoxide.

Results to Date:

For surface workers, there was a more marked decrease in functional values in smokers than in nonsmokers, but the decrease was similar for active and retired subjects within each smoking category. For underground workers, the decrease was more marked in active workers (smokers and nonsmokers); however, whether active or retired, the decrease was always more marked in smokers than in nonsmokers. Between the two surveys, 121 smokers stopped smoking. Although they were older than those who continued to smoke, decreases of VC, FEV_1, and FEV_1/VC were less.

Project Dates:

May 1980–completed.

Financial Support:

Commission of European Communities (7246-24-008).

0222. INSERM UNIT 14, INSTITUT NATIONAL SANTE ET RECHERCHE MEDICALE, CHU Brabois, 54511 Vandoeuvre Cedex, France.

Project Title:

Factors Influencing the Pulmonary Function in Children and Adolescents.

Principal Investigators:

Teculescu, B.D.; Pham, Q.T.

Objective:

To identify factors (sex, age, body build, personal and passive smoking, genetic factors, familial environment) that influence pulmonary function in children and adolescents aged 10 to 16 years.

Methods or Approach:

Subjects were 534 children selected at random from those attending a Preventive Medicine Center for routine health checkup. A standard respiratory symptom questionnaire was administered to one of the parents. A forced expirogram for children automatically computed forced vital capacity, forced expiratory volume in 1 sec, mean maximal expiratory flow, and mid-expiratory flow (MEF) at 75, 50, 25 percent vital capacity. Single breath nitrogen washout (nitrograph/pneumotachograph/programmed computer) was used to compute lung volumes, phase III slope, and closing volume.

Results to Date:

Description of the apparatus assembly and the computing system used has been submitted for publication. Preliminary analysis showed that about one in five children was unable to correctly perform the sequence of maneuvers required for completion of two valid nitrogen washouts (slow full inspiration, slow complete expiration with uniform flow). The variability of phase III slope, lung volume, and closing volume determinations is superior to that of indices derived from the forced expirogram, with the exception of MEF_{25} percent (to be expired) vital capacity.

Future Plans:

Smoking habits will be studied during followup of the sample.

Project Dates:

December 1982–December 1983.

Financial Support:

INSERM.

0223. INSERM UNIT 14, INSTITUT NATIONAL SANTE ET RECHERCHE MEDICALE, 54511 Vandoeuvre Cedex, France.

Project Title:

Longitudinal Study of Pulmonary Function in Male Smokers.

Principal Investigators:

Teculescu, D.B.; Pham, Q.T.

Objective:

To (1) examine pulmonary function in asymptomatic male smokers aged 35 to 55 years in 1979; (2) establish predictive value of small airway tests for development of airflow obstruction; and (3) study pulmonary function in subjects who stop smoking.

Methods or Approach:

The study cohort was comprised of males attending a center for preventive medicine. Methods used included (1) standard questionnaire of respiratory symptoms; (2) spirometry (vital capacity (VC) and forced expiratory volume in 1 sec (FEV_1) with a wet spirometer); (3) plethysmography (TGV, residual volume (RV), total lung capacity (TLC), SGaw) with constant volume plethysmograph); (4) diffusing capacity (DL), DL/alveolar ventilation (VA), and VA' with Morgan transfer test apparatus; (5) single breath N_2 washout test, phase III slope, and closing volume/VC with nitrograph, bag in box, and spirometer; and (6) lung volume (V)/V curves with air and 80 percent He-20 percent O_2, mid expiratory flow at 75, 50, and 25 percent VC, helium-to-air difference in flow at 50 percent and 25 percent VC, and volume isoflow.

Results to Date:

Results indicate that (1) He and air V/V curves must be carefully handled to obtain reliable information; (2) there is no correlation between ΔHe_{50} and amount smoked; (3) sex and body build do not influence density dependence; (4) acute upper respiratory tract infections may alter permeability of peripheral airways; and (5) previous smokers have borderline normal results on small airways tests.

Future Plans:

Followup will be conducted after 5 years.

Project Dates:

February 1979–December 1985.

Financial Support:

INSERM.

References:

(1) Teculescu, D.B.; Pino, J.; Sadoul, P. "Cigarette Smoking and Density-Dependence of Maximal Expiratory Flow in Asymptomatic Men." *American Review of Respiratory Disease* 122(4):651-656, 1980. (2) Teculescu, D.B.; Pham, Q.T.; Locuty, J., et al. "Episode Infectieux Respiratoire Banal et Obstruction des Voies Aeriennes Peripheriques." (Common Respiratory Tract Infection and Peripheral Airway Obstruction.) *Clinical Respiratory Physiology* 19(4):393-399, 1983, French.

0224. INSERM UNIT 14, INSTITUT NATIONAL DE RECHERCHE ET DU SECURITE, 54500 Vandoeuvre Cedex, France.

Project Title:

Effect of Smoking on the Concentration and Activity of Human Serum Alpha-1 Antitrypsin According to Phenotype Pi.

Principal Investigators:

Pierre, F.; Goutet, M.; Mur, J.M., et al.

Objective:

To evaluate effect of cigarette smoking on concentration and activity of α_1-antitrypsin according to genetic characteristics (Pi).

Methods or Approach:

In an epidemiological study of pulmonary function in 1,100 iron miners (aged 35 to 60 years) smoking habits were noted by questionnaire and venous blood was taken for characterization of phenotype Pi and evaluation of concentration and activity of α_1-antitrypsin. Phenotypes were determined by analytical electrofocusing on polyacrylamide gel in pH gradient 4.2 to 5.3. Concentration of α_1-antitrypsin was quantified by electroimmunodiffusion. Activity of α_1-antitrypsin was measured by inhibition of swine pancreatic elastase.

Results to Date:

Among the 1,100 miners, 73 had phenotype Pi MS and 24 had phenotype MZ or S. Mean concentration and mean activity of α_1-antitrypsin were significantly lower in MS and MZ groups than in the MM group; 70 percent for MS and 50 percent for MZ and S. Activity of the molecule of α_1-antitrypsin (elastase inhibitory capacity, EIC) was not significantly different for M, MS, or MZ groups. In each of the groups (M, MS, and MZ), concentrations of α_1-antitrypsin and EIC were higher in smokers than in nonsmokers and ex-smokers, and higher in heavy smokers than in light smokers; however, activity of the α_1-antitrypsin molecule was not affected by smoking habits.

Future Plans:

A similar study is being conducted in a cohort of 1,200 other workers to verify results.

Project Dates:

May 1980–1986.

Financial Support:

INSERM.

0225. INSERM UNIT 169, 94807 Villejuif Cedex, France.

Project Title:

Infantile Colic and Parental Smoking.

Principal Investigators:

Said, G.; Patois, E.; Lellouch, J.

Objective:

To determine the relationship between evening and postprandial colic and parental smoking.

Methods or Approach:

The study group consisted of 253 infants examined at the routine pediatric consultation at 3 months of age. Mothers were interviewed and four digestive symptoms were recorded; regurgitation, vomiting, flatus, and crying after meals. Other questions concerned parity, birth weight, method of feeding, conditions of delivery, and socioeconomic status, education, and smoking habits of parents.

Results to Date:

Postprandial and evening colic occurred independently; postprandial colic was related to other digestive symptoms, but evening colic was not. Parental smoking was associated with digestive symptoms, and particularly with postprandial colic, but not with evening colic. Postprandial colic was strongly related to parental smoking, method of infant feeding, and socioeconomic status. Parity, birth weight, and conditions of delivery were not associated with either postprandial colic or evening crying. Young babies are probably more susceptible to an environment polluted by smoke or the odor of stale tobacco because of their sensitive olfactogustatory systems. It may be hypothesized that gastrointestinal contractions are triggered by olfactory or gustatory stimulation through a vagal reflex mechanism. Whatever the true cause of infantile colic, it may benefit families to know that parental smoking may be a factor.

Reference:

Said, G.; Patois, E.; Lellouch, J. "Infantile Colic and Parental Smoking." *British Medical Journal* 289:660, September 15, 1984.

0226. INSERM UNIT 179, 44 Chemin de Ronde, 78110 Le Vesinet, France.

Project Title:

Can the Results of Pulmonary Function Tests and Evidence of Smoking-Related Respiratory Symptoms Be Used to Dissuade the Young From Smoking?

Principal Investigators:

Neukirch, F.; Cooreman, J.; Perdrizet, S.

Objective:

To determine whether the finding of a decrease in pulmonary function values and evidence of smoking-related symptoms in a sample of adolescents can be used to persuade young people to reduce cigarette consumption.

Methods or Approach:

In 1978, 2,269 pupils of a Paris state secondary school completed self-administered questionnaires about respiratory symptoms and diseases and smoking habits. A random sample of 970 also had a spirography and a flow/volume curve, and each participant was given the results, with a short comment. At the end of the school year, a conference was organized and researchers showed that among smokers, prevalence of respiratory symptoms was higher and average functional values were lower than in nonsmokers. Two years later, 48 students with diminished respiratory function and 157 representative controls were re-examined. Pupils reported any modifications in cigarette consumption.

Results to Date:

Among the 205 pupils seen in 1980, 55 were smokers and 53 had exploitable flow/volume curves and spirometry. Between 1978 and 1980, 17 had reduced cigarette consumption (group D) and 37 had not (group A). Results showed that (1) average consumption in 1978 was 10.5 cigarettes/day for group D and 5.3 cigarettes/day for group A; (2) prevalence of usual cough was higher in group D; and (3) average values of flow and volume measured in 1978 were lower in group D (those who reduced consumption between 1978 and 1980). Results suggest that evidence of objective troubles related to smoking could be used as arguments in antismoking campaigns among adolescent students.

Project Dates:

1978–1984.

Financial Support:

INSERM (CRL 79 52955).

0227. INSERM UNIT 21, 16 Avenue Paul Vaillant Couturier, 94807 Villejuif Cedex, Paris 75231, France.

Project Title:

Epidemiological Study of Factors Affecting Human Fecundity.

Principal Investigators:

Spira, A.; De Mouzon, J.; Schwartz, D.

Objective:

To study factors related to human fertility; determine distribution of fecundity among couples and effects of age, smoking, and previous contraception.

Methods or Approach:

A cohort of 2,000 volunteer couples were followed for 12 months after cessation of contraception to promote pregnancy. Basal body temperature (BBT) charts were completed every month until pregnancy.

Results to Date:
Mean fertility is estimated to be about 32 percent. Spontaneous abortion rate is rather low (11.5 percent) and there is a close relationship between some BBT chart parameters (length of hypothermic phase) and occurrence of congenital malformations. Preliminary results seem to indicate decreased fecundity among smokers (men and women).
Project Dates:
1979–1986.
Financial Support:
INSERM.

0228. INSERM UNIT 287, INSTITUTE GUSTAVE ROUSSY, Departement de Statistique Medicale, Rue Camille Desmoulins, 94805 Villejuif Cedex, France.

Project Title:
Lung Cancer and Use of Tobacco: A French Case–Control Study.

Principal Investigators:
Benhamou, S.; Benhamou, E.; Flamant, R.
Objective:
To (1) refine the study of risk factors for lung cancer; (2) examine risk factors according to sex and histological type; (3) study the association between lung cancer and different smoking habits (cigarettes, cigars, pipe); and (4) examine association between lung cancer and type of tobacco used (light or dark), use of filtered or nonfiltered cigarettes, and use of handrolled or manufactured cigarettes.
Methods or Approach:
In the case–control study, conducted simultaneously in France and in four other European countries, 1,625 cases and 3,091 controls from France were included. All cases had histologically confirmed lung cancer, diagnosed less than 1 year before interview. Controls, two for each case (matched by sex, age at diagnosis, hospital of admission, and interviewer), were patients hospitalized for nontobacco diseases. This requirement excluded patients with cancers of the respiratory tract, esophagus, liver, pancreas, bladder, and kidney, and patients with myocardial infarction, other cardiovascular diseases, gastric ulcer, chronic bronchitis, and alcoholic cirrhosis. Questionnaires contained items about place of residence since birth, educational level, occupation, smoking, and drinking habits. Lung cancer risks were estimated by matched logistic regression analysis.
Results to Date:
The first association studied was the association between Kreyberg I and Kreyberg II lung cancer and type of cigarettes smoked (filter or nonfilter, manufactured or handrolled, light or dark tobacco). Results are based on 1,217 cases and 1,915 controls (all nonsmokers or exclusively cigarette smokers). Relative risk (RR) of lung cancer was significantly increased with certain indices of duration and intensity of cigarette exposure, including early age for first cigarette smoked, daily consumption, frequency of inhalation, and duration of smoking. When all covariates were taken into account in matched logistic regression (excluding nonsmokers), lung cancer RR for nonfilter vs. filter cigarette smokers was 1.23; for handrolled vs. manufactured cigarette smokers, 1.22; and for dark vs. light tobacco users, 1.94.
Project Dates:
1976–1985.
Financial Support:
NCI (NO1-CP-05642).

0229. INSERM UNIT 63, 22 Avenue du Doyen Lepine, 69 500 Bron, France.

Project Title:
Effect of Smoking and Dietary Saturated Fats on Platelet Functions in Scottish Farmers.

Principal Investigators:
Renaud, S.; Dumont, E.; Baudier, F., et al.
Objective:
To determine whether the effect of smoking on platelet functions is additive to the untoward effect of saturated fats.
Methods or Approach:
Effect of smoking one high tar/high nicotine cigarette was compared in farmers (smokers, inhalers) from East and West Scotland. Blood was taken in fasted subjects, deprived of smoking since the day before, and 10 minutes after smoking a cigarette. Coagulation and platelet aggregation induced by thrombin and epinephrine were evaluated before and after smoking. A survey of dietary habits (chemical analysis, weighting technique, past recall) was also performed for each subject and serum lipids were analyzed.
Results to Date:
In the West group, intake of dairy fats and saturated fats, P/S ratio, and most of the platelet function tests estimated were significantly higher than in the East group. Serum cholesterol (total and high density lipoprotein) levels were similer, although triglycerides were lower in the West. Smoking one cigarette enhanced platelet functions in both areas, but increases were more marked in the West group. The increase in platelet response to smoking was additive to that induced by saturated fat intake; platelet response to thrombin and epinephrine after smoking one cigarette in the West group was approximately four times the response obtained before smoking (or in a nonsmoker) in the East. The additive effects of cigarettes and saturated fat might be relevant to the reported higher incidence of coronary heart disease in the West of Scotland.
Project Dates:
1979–1982.
Financial Support:
INSERM; Canadian Tobacco Council.

0230. INSERM UNIT 63, 22 Avenue du Doyen Lepine, 69 500 Bron, France.

Project Title:
Platelet Function After Cigarette Smoking in Relation to Nicotine and Carbon Monoxide.

Principal Investigators:
Renaud, S.; Blache, D.; Dumont, E., et al.
Objective:
To (1) determine whether cigarette smoking has an effect on blood coagulation, platelet aggregation, and platelet clotting activity; (2) observe whether effect is related to nicotine (and tar) yields of cigarettes; (3) determine whether effect is related to level of nicotine and carbon monoxide (CO) in blood; and (4) determine whether effect could be reproduced by in vitro addition of nicotine to platelet-rich plasma (PRP).
Methods or Approach:
Blood was taken from fasted smokers (deprived of smoking since the day before) before and 10 minutes after smoking a cigarette delivering 0.07, 0.18, 0.4, 0.58, or 1.44 mg nicotine to determine coagulation (recalcification plasma clotting time); clotting activity of platelets; platelet aggregation to thrombin, ADP, collagen, and epinephrine; and CO and nicotine in blood. Nicotine, at levels comparable to those found in blood,

was also added in vitro to platelet rich plasma to determine effect on coagulation and platelet aggregation.

Results to Date:

Increase in platelet aggregation to thrombin, adenosine diphosphate, collagen, and epinephrine ranged from 0 percent to approximately 80 percent for cigarettes with higher nicotine yields. Blood nicotine levels increased from 112 percent to 644 percent. Clotting activity of PRP and platelets rose by 16 percent with cigarettes with highest nicotine content. Platelet activity correlated with blood nicotine levels, but not with carboxyhemoglobin levels. Nicotine diluted in saline solution and added in vitro to PRP from six other subjects 2 minutes before aggregation or clotting test at levels after smoking (10 to 20 ng/mL) induced a increase in platelet reactivity of the same order as that after smoking cigarettes. Data suggest that in some cigarettes, nornicotine and substances contained in tar may contribute to effect of cigarette smoking on platelets.

Future Plans:

Research will continue to determine whether substances in cigarette smoke other than nicotine are able to influence platelet functions.

Project Dates:

1978–1982.

Financial Support:

INSERM; Canadian Tobacco Council.

Reference:

Renaud, S.; Blache, D.; Dumont, E., et al. "Platelet Function After Cigarette Smoking in Relation to Nicotine and Carbon Monoxide." *Clinical Pharmacology and Therapeutics* 36(3):389-395, September 1984.

0231. INSERM, Statistical Research Unit, 16 Bis rue Paul-Vaillant-Couturier, 94800 Villejuif, France.

Project Title:

Variations in Mortality for Some Types of Cancer in Relation to Alcohol and Tobacco Consumption in France.

Principal Investigator:

Sancho Garnier, H.

Objective:

To analyze the effects of alcohol and tobacco consumption on the mortality rates for cancer of some specific sites, using geographical correlations and discussing the evolution of those correlations over time.

Methods or Approach:

The study covers the last three decades in the 95 French counties. Strong regional contrasts in the factors under study, and differences between male and female exposures will facilitate this type of analysis. A comparison will be made between effects measured at the individual level and those measured by geographical correlations for cancer sites, such as oral cavity and pharynx, larynx, lung, and esophagus, which have been the objects of case–control studies. Examination of the combined effects of alcohol and tobacco on other cancer sites (e.g., digestive tract, bladder, or breast cancer) will then be carried out. In addition, this study will allow the evaluation of the effects of some other environmental factors.

Results to Date:

Data collection has been completed and statistical analysis is currently being carried out. A preliminary report was made in April 1983.

Project Dates:

1980–1982.

Financial Support:

Haut Comite d'Etude et d'Information sur l'Alcoolisme.

0232. INSERM, Unit 179, 44 Chemin de Ronde, 78110 Le Vesinet, France.

Project Title:

Tar and Nicotine Levels of the Cigarettes Smoked by Teenagers, and Anti-Smoking Campaign.

Principal Investigators:

Cooreman, J.; Burghard, G.; Perdrizet, S.

Objective:

To assess the influence of different methods used in an antismoking campaign on tar and nicotine levels of the cigarettes smoked by 10,000 teenagers aged 14 to 18.

Methods or Approach:

The data collection was double: a questionnaire sent to school principals determined if and how an antismoking action had been carried out during the last 2 years, and a self-administered questionnaire filled in at school by teenagers examined quantity and the brand of cigarettes smoked, the length of butt ends left, and the antismoking information received from the mass media.

Results to Date:

The teenagers who smoked a greater number of cigarettes per day smoked brands with higher levels of tar and nicotine. The tar and nicotine level was lower if the campaign had been carried out by means of posters, if a teacher was responsible, and if only one antismoking action had been carried out in the school. No significant relationship was found between tar and nicotine levels and mass media campaigns. Study results have been published.

Project Dates:

April 1979–1982.

Financial Support:

INSERM; Delegation Generale a la Recherche Scientifique et Technique Decision d'aide (N78-7-0595).

Reference:

Cooreman, J.; Burghard, G.; Perdrizet, S. "Tar and Nicotine Levels of the Cigarettes Smoked by Teenagers, and Anti-Smoking Campaign." *Bulletin of the International Union Against Tuberculosis* 59(1/2):40-43, 1984.

0233. INSERM, Unit 179, 44 Chemin de Ronde, 78110 Le Vesinet, France.

Project Title:

Prevention of Smoking in Primary School.

Principal Investigators:

Cooreman, J.; Perdrizet, S.; Burghard, G.

Objective:

To demonstrate the relative effectiveness of educational antismoking measures when information is given to specific age groups.

Methods or Approach:

A retrospective study was made from a self-administered questionnaire distributed to 4,166 pupils aged 15 to 18, attending Bas-Rhin high schools, in spring 1979. The questions were about smoking habits and behavior as well as the age at which antismoking information had been received.

Results to Date.

The proportion of smokers was significantly lower if the information had been received in primary school (22.5 percent) than if it had been received in lower secondary school (25.2 percent) or in upper secondary school (34.9 percent). The boys smoked fewer cigarettes per day, and chose brands with lower tar and nicotine levels if the information had been received in primary school. Among those informed in primary school, 2.9 percent of male and female smokers left 3/8 of the cigarette unsmoked, whereas only 1.6 percent of those informed in lower secondary school and 1.4 percent of those informed in upper secondary school did so. The proportions of pupils who wished to give up and of those who had never smoked were higher among those who had been informed in primary school. Results have been published.

Project Dates:
April 1979–1982.

Financial Support:
INSERM; Delegation Generale a la Recherche Scientifique et Technique Decision d'aide (N78-7-0595).

Reference:
Cooreman, J.; Perdrizet, S.; Burghard, G. "La Lutte Anti-Tabagique a l'Ecole Primaire." *Archives Francaises de Pediatrie* 39(2):113-117, 1982.

0234. INSERM, Unit 179, 44 Chemin de Ronde, 78110 Le Vesinet, France.

Project Title:
Prevalence of Respiratory Symptoms in Parisian Teenagers According to Smoking Habits.

Principal Investigators:
Neukirch, F.; Liard, R.; Cooreman, J., et al.

Objective:
To determine whether women are more vulnerable to the effects of smoking on respiratory symptoms than men in adolescence.

Methods or Approach:
A survey was carried out in a Paris state secondary school in October 1978. The 2,266 students present (mean age 14.9 years) completed a self-administered questionnaire derived from the standard Medical Research Council questionnaire (respiratory symptoms and diseases, and smoking habits). A random sample of 970 were then examined by measuring forced expiratory volume in 1 second (FEV_1) using a dry spirometer.

Results to Date:
Among nonsmokers, the proportion of those with cough and/or phlegm was the same in both sexes (26 percent), but among current smokers 44.7 percent of the girls had these respiratory symptoms compared to 34.9 percent of the boys. The girls had a higher proportion of affirmative responses to both cough and/or phlegm and wheezing at every level of cigarette smoking above a total of 4,000 cigarettes. Among boys the correlation between total cigarettes ever smoked and $FEV_1/Height^3$ was $\eta = +0.13$, and among girls $\eta = -0.21$. Thus there was a weak but significant association between total cigarettes smoked and respiratory function in girls.

Project Dates:
October 1978–1982.

Financial Support:
INSERM (CRL 79-5-29-55).

Reference:
Neukirch, F.; Liard, R.; Cooreman, J., et al. "Prevalence of Respiratory Symptoms in Parisian Teenagers According to Smoking Habits." *Journal of Epidemiology and Community Health* 36:202-204, 1982.

0235. INSERM, Unit 179, 44 Chemin de Ronde, 78110 Le Vesinet, France.

Project Title:
Effects of Antismoking Actions in a Population of 10,000 Teenagers.

Principal Investigators:
Cooreman, J.; Perdrizet, S.; Burghard, G.

Objective:
To compare the proportion of smokers between the schools where antismoking actions have been carried out and others where such actions have not been carried out; appraise the different methods applied.

Methods or Approach:
A questionnaire has been sent to school principals to find out if antismoking actions have been carried out (once or twice) in their schools, by what means, within what scope, and who had participated. A self-administered questionnaire, filled in at school by all the teenagers simultaneously, asked smokers questions about the quantity and the brand of cigarettes smoked, the reasons for smoking, the age when they had begun smoking, possible modifications in their cigarette consumption during the last 2 years, and their possible wish to give up smoking. All the teenagers were asked their opinions about the discomfort caused by smoking and if they had been informed of the risks due to smoking.

Results to Date:
One antismoking campaign has been conducted in 76 percent of the secondary schools surveyed (only 10 percent of the schools had two campaigns). The strategies included use of posters and instruction from teachers, with the help of the Committee for Health Education or the Committee Against Respiratory Diseases. Data show that 26 percent of pupils said they regularly smoke 8.5 cigarettes/day containing an average of 15.7 mg of tar and 1.03 mg of nicotine. A total of 997 pupils wished to give up smoking; 671 had already seriously tried to quit. Nearly all of them (85 percent) acknowledged the discomfort caused by smoking and approved of the governmental restrictions. As for the risks due to smoking, 64 percent of pupils had received information in class and 93 percent from mass media. In campaigns carried out in secondary schools, the results were encouraging if done by means of posters and if a teacher was responsible. If we consider the total information received by pupils during the whole of their school-life, the quit-rate and the proportion of pupils having tried to persuade their peers to give up smoking were higher among those who had received at least two campaigns. The proportion of current smokers was definitely lower among those who had been informed in primary school. Results have been published.

Project Dates:
April 1979–1981.

Financial Support:
INSERM; Delegation Generale a la Recherche Scientifique et Technique.

Reference:
Cooreman, J.; Perdrizet, S.; Purghard, G. "Effects of Antismoking Actions in a Population of 10,000 Teenagers." *Medecine et Hygiene* 43(14):1466-1475, 1983.

0236. INSERM, Unit 179, 44 Chemin de Ronde, 78110 Le Vesinet, France.

Project Title:
Influence of Parents on Their Children's Smoking Habits.

Principal Investigators:
Neukirch, F.; Cooreman, J.

Objective:
To study the precocity and prevalence of smoking in young people according to their parents' smoking habits and attitudes.

Methods or Approach:
A survey was administered in October 1978 in a Parisian

secondary school with 2,266 pupils (mean age 14.9 years). Students completed a self-administered questionnaire about respiratory symptoms and diseases, their smoking habits, and their parents' smoking habits and attitudes about smoking.

Results to Date:

Survey data showed that 21.8 percent of the boys and 31.2 percent of the girls were smokers. These proportions varied according to the attitudes of parents: they were lower if the parents forbade children to smoke and higher if they just recommended that children not smoke or if they permitted children to do so. Moreover, the proportion of smokers and the precocity of smoking increased with parents' smoking habits. These results were confirmed by a discriminant analysis which brought out the importance of the variable "Parents' consent to their children's smoking." Results have been published.

Project Dates:

October 1978–1982.

Financial Support:

INSERM (CRL 79-5-29-55).

Reference:

Neukirch, F.; Cooreman, J. "Influence of Parents on Their Children's Smoking Habits." *Social Science and Medicine* 17(11):763-769, 1983.

0237. INSERM, Unit 149, 16 Avenue Paul Vaillant Couturier, 94807 Villejuif, France.

Project Title:

Tobacco and Alcohol in Pregnancy and Fetal Outcome.

Principal Investigators:

Kaminski, M.; Lelong, N.; Du Mazaubrun, C.

Objective:

To study the morphological and behavioral characteristics of infants at birth in relation to alcohol and tobacco use by the mother before and during pregnancy.

Methods or Approach:

Data will be collected prospectively beginning with the first visit of pregnant women to the participating hospitals. Babies will be examined (blind) for maternal characteristics such as alcohol and tobacco use. The survey will begin in April 1985.

Results to Date:

Project is in a preliminary phase.

Project Dates:

1985–1987.

Financial Support:

Haut Comite d'Information et d'Etude sur l'Alcoolisme; INSERM.

0238. INSERM, Unit 149, 16 Avenue Paul Vaillant Couturier, 94807 Villejuif, France.

Project Title:

Trends in Smoking During Pregnancy and Effects on Birthweight.

Principal Investigators:

Kaminski, M.; Lelong, N.; Cornuau, P.

Objective:

To monitor tobacco use by pregnant women; investigate effects of the increase in smoking on outcome of pregnancy.

Methods or Approach:

Data used were collected in three national surveys (1972, 1976, and 1981) of births in France. Information on tobacco use before and during pregnancy and on social and medical characteristics of mothers was collected by interview after the birth. Characteristics of infants were extracted from medical records. Tobacco use, as indicated in the three surveys, was compared, as were characteristics of smokers. Birth outcome analysis, according to tobacco use, took into account social modifications between 1972 and 1981.

Results to Date:

The proportion of women who smoked before and during pregnancy increased between 1972 and 1981, particularly in lower social groups where smoking was rare in 1972. The increase in tobacco use might partially explain the observation that, while frequency of preterm deliveries decreased between 1972 and 1981, birth weight increased only marginally, and only for nonsmokers.

Project Dates:

1972–1985.

Financial Support:

French Department of Health; INSERM.

0239. INSERM, Statistical Research Unit, 16 Avenue Paul Vaillant Couturier, 94807 Villejuif Cedex, France.

Project Title:

Prevalence of Smokers Among Diabetics and Influence of Tobacco on Diabetic Retinopathy.

Principal Investigators:

Lombrail, P.; Eschwege, E.; Passa, P.

Objective:

To study prevalence of tobacco smoking among diabetic patients; evaluate influence of smoking in prevalence of diabetic retinopathy.

Methods or Approach:

In a cross-sectional study of 647 diagnosed diabetics recruited in a diabetology clinic, patients completed a questionnaire about smoking habits. All patients had had retinal angiography in the year preceding the study. A prospective study was conducted on prevention (or delay) of diabetic retinopathy by antiplatelet agents. Information about tobacco consumption is collected regularly.

Results to Date:

Results of the cross-sectional study showed that 35 percent of the patients were habitual smokers, 20 percent were exsmokers, and 45 percent were nonsmokers. Smoking had no effect on prevalence or severity of diabetic retinopathy. Data collection in the prospective study has been completed and findings are being analyzed. Results will be presented in 1985.

Project Dates:

1983–1984.

Financial Support:

INSERM.

0240. INSERM, UNIT 179, 44 Chemin de Ronde, 78110 Le Vesinet, France.

Project Title:

Smoking Habits and Respiratory Symptoms in Adolescents Living in Bordeaux.

Principal Investigators:

Cooreman, J.; Perdrizet, S.; Levallois, M.

Objective:

To study the relationship between adolescent smoking habits and respiratory symptoms; attempt to confirm the relationship with pulmonary function tests.

Methods or Approach:

The survey was conducted in spring 1981 among 15,247 adolescent schoolchildren (47 percent boys); average age was 16.5 years. Data were collected during class (self-administered questionnaire) on smoking habits and respiratory symptoms and history. Respiratory function tests were conducted on a random sample of 172 students (spirometry, forced vital capacity, forced expiratory volume in 1 sec, and forced mid-expiratory flow).

Results to Date:

Smoking prevalence was 37.1 percent among boys and 43.2 percent among girls; most (87.0 percent) smoked filter-tipped cigarettes. Boys began smoking regularly at 14.9±1.5 years of age and smoked an average of 9.5±6.5 cigarettes/day. Girls began smoking regularly at 15.0±1.4 years of age and smoked 8.0±5.3 cigarettes/day. Except for asthma, there was a statistically significant ($p < 0.001$) relationship between adolescent smoking and current respiratory symptoms.

Future Plans:

Analysis of spirometric values according to smoking habits is in progress.

Project Dates:

January 1981–December 1985.

Financial Support:

National Committee Against Respiratory Diseases and Tuberculosis, France.

0241. INSTITUT D'ETUDES ET RECHERCHES PNEUMOPHTISIOLOGIQUES, (Institute of Studies on Pulmonary Tuberculosis), Sainte-Marquerite Hospital, 270 Boulevard de Sainte-Marquerite, 13009 Marseille, France.

Project Title:

Longitudinal Study of the Methods of Early Detection of Respiratory Diseases in a Population of Cab Drivers.

Principal Investigators:

Kleisbauer, J.P.

Objective:

To (1) evaluate the distribution of spirometric parameters in a population of cab drivers; (2) investigate the correlation of the spirometric values with risk factors such as occupation, tobacco use, and heredity; and (3) follow up the study population to develop tests better able to predict lung disease.

Methods or Approach:

The study group will consist of 200 cab drivers who will be asked questions on lung symptoms and lung disease. Studies will be conducted to determine flow-volume curve of nitrogen washout; genetic study of α_1-antitrypsin; and level of lead and cadmium in serum. In the first phase, 108 cab drivers were studied. Lung volume parameters were found to decrease with age, but there was no significant modification related to tobacco consumption. Chronic bronchitis was found in 3 percent of cases.

Project Dates:

April 1981–1988.

Financial Support:

INSERM (810123); Institut d'Etudes et Recherches Pneumophtisiologiques; Securite Sociale, France.

0242. INSTITUT DE PROTECTION ET DE SURETE NUCLEAIRE, Departement de Protection Sanitaire, B.P. 6, 92260 Fontenay-aux-Roses, France.

Project Title:

Epidemiological Study of Uranium Miners in France.

Principal Investigators:

Tirmarche, M.; Piechowski, J.; Chameaud, J.

Objective:

To determine cancer mortality in a cohort of uranium miners; study the relationship with exposure to radon daughters.

Methods or Approach:

Uranium miners entering the study had been employed as underground miners for at least 3 months between 1947 and 1972. Mortality will be compared with national mortality for males during the same period. Besides exposure to radon daughters, tobacco consumption and previous employment will be taken into account.

Results to Date:

Preliminary results indicate a standardized mortality ratio for lung cancer of 1.8, statistically significant at $p < 0.001$.

Project Dates:

1981–continuing.

Financial Support:

Institut de Protection et de Surete Nucleaire.

0243. INSTITUT NATIONAL DE RECHERCHE ET DE SECURITE, Avenue de Bourgogne, BP 27, 54501 Vandoeuvre Cedex, France.

Project Title:

Environment, Occupation, and Lung Cancer: A Methodological Approach.

Principal Investigator:

Moulin, J.-J.

Objective:

To quantify the causality of tobacco and occupation in occurrence of lung cancer.

Methods or Approach:

Standard mortality ratios, standard incidence ratios, proportional incidence ratios, and odds ratios, for tobacco-related cancers, will be compared among specific occupational groups. Data will be derived from (1) Registrar General's decennial supplement for England and Wales (1970-1972), (2) Swedish Cancer Environment Registry (1961-1973), Third National Cancer Survey Interview, and a literature review.

Results to Date:

Mortality (or incidence) rates for oral cavity and laryngeal cancer are considered to be the result of tobacco consumption. Similar rates for lung cancer are related to tobacco consumption and occupational exposures. Comparison of figures are consistent with the hypothesis of incidence of occupational lung cancer higher than common estimations (5 percent).

Project Dates:

September 1982–December 1985.

Financial Support:

Institut National de Recherche et de Securite, France.

0244. INSTITUT NATIONAL DE RECHERCHE ET DE SECURITE, Avenue de Bourgogne, BP 27, 54501 Vandoeuvre Cedex, France.

Project Title:

Comparative Epidemiology, In Europe, of Tobacco-Related Cancers (Lung, Larynx, Pharynx, Buccal Cavity).

Principal Investigators:

Moulin, J.-J.; Mur, J.-M.; Cavelier, C.

Objective:

To compare geographical distribution and secular trends of tobacco-related cancers in Europe; test the hypothesis that tobacco smoke is a major causative factor of cancer of the respiratory tract and of the oral cavity.

Methods or Approach:

Available data on male age-adjusted mortality rates (World Health Statistics, WHO) and male age-adjusted incidence rates (Cancer Incidence in Five Continents, WHO) in European countries, from 1950 to 1977, were utilized. Geographical correlation coefficients were computed, at different times, between lung cancer mortality (or incidence) and laryngeal or oral cavity cancers. Secular trends in mortality are compared.

Results to Date:

No significant geographical correlation between lung and upper respiratory tract cancer was found and there does not appear to be any relationship between secular trends. All countries experienced a sharp increase in lung cancer mortality; laryngeal and oral cavity cancers showed divergent trends (10 countries had steady or decreasing rates). Results suggest that tobacco may not be the major causative factor for laryngeal and oral cavity cancers.

Future Plans:

The project may be extended to consider female sex and cancers of the bladder and esophagus.

Project Dates:

January 1983–December 1985.

Financial Support:

Institut National de Recherche et de Securite, France.

0245. INTERNATIONAL AGENCY FOR RESEARCH ON CANCER, 150 Cours Albert-Thomas, 69372 Lyon, France.

Project Title:

An International Study of Urinary Cotinine Levels in Nonsmokers.

Principal Investigators:

Preston-Martin, S.; Saracci, R.; O'Neill. I.

Objective:

To (1) investigate relationship between questionnaire responses (smoking status and passive smoking exposure) and levels of urinary cotinine in nonsmokers; (2) relate cotinine levels in nonsmoking women to smoking status of husband or other household members and to tobacco smoke exposure outside the home, particularly at work; and (3) compare urinary cotinine levels of nonsmoking women in various countries including Japan, Greece, and the United States, taking into account exposure to passive smoking at home and elsewhere.

Methods or Approach:

Subjects will be women for whom questionnaire data on smoking and passive smoking are already available. Each participating center will be asked to select 100 nonsmoking women. If numbers permit, 50 of the women are to be currently married to a smoker and the other 50 not currently living in the same household with a smoker. If possible, each group will be further divided according to the woman's reported exposure to passive smoking outside the home. Each subject will be reinterviewed to obtain current data on smoking status, including usual passive smoking exposure at home, and work, and elsewhere and specific active and passive exposures during the preceding week. Subjects will be asked to provide a urine sample. Details of primary exposure situations, including size and ventilation of the room and proximity to the smoker, will also be obtained. Cotinine and creatinine levels in urine samples will be measured and cotinine levels will be standardized according to amount of creatinine present.

Results to Date:

Project is in a preliminary phase.

Project Dates:

1985–1987.

Financial Support:

IARC.

0246. INTERNATIONAL AGENCY FOR RESEARCH ON CANCER, Division of Epidemiology and Biostatistics, 150 Cours Albert Thomas, 69372 Lyon, Cedex 08, France.

Project Title:

Collaborative Case-Control Study of Cancers of the Pancreas, Bile-Duct, and Gallbladder.

Principal Investigator:

Walker, A.M.

Objective:

To study the etiology of cancers of the pancreas, gallbladder, and bile-duct; collect data on a variety of known or candidate risk factors (including tobacco consumption) to control for confounding in the analysis and to evaluate older observations.

Methods or Approach:

Principal hypotheses are that (1) regular exposure to stimulators of cholecystokinin release predisposes to pancreatic cancer; (2) fats from animal sources carry risks that are identifiably different from those associated with fats from vegetable sources; (3) timing and variability of food consumption are risk factors for disease, over and above the simple effects of total quantity of exposure; and (4) diabetes associated with pancreatic cancer has age at onset and insulin dependence patterns reflective of chronic islet cell toxicity. Population-based case–control studies are simultaneously being carried out in Australia, Canada, the Netherlands, and Poland. An agreed-upon set of questions is administered in each center. Information is sought on frequency and duration of use of plain cigarettes, hand-rolled plain cigarettes, low-tar cigarettes, other filter cigarettes, cigars, cigarillos, pipes, and chewing tobacco. Changes in habits throughout the life-span are recorded in detail. Other questions concern consumption of coffee, tea, and alcoholic beverages, and subject's medical history, including use of various drugs. In addition, a dietary questionnaire, adapted to locally existing dietary patterns, is administered. At least 800 cases will be enrolled.

Results to Date:

Results are not yet available.

Project Dates:

November 1983–December 1986.

0247. LABORATOIRE D'IMMUNOLOGIE ET D'ALLERGOLOGIE, 5, Boulevard du Montparnasse, 75006 Paris Cedex, France. P.O. BOX 1951, 4001 Basle 1, Switzerland.

Project Title:

Nicotine As a Hapten in Seborrhoeic Dermatitis.

Principal Investigators:

Sudan, B.J.L.; Sainte-Laudy, J.; Sterboul, J.

Objective:

To (1) detect a reaction of hypersensitivity to nicotine as a hapten in patients afflicted with seborhoeic dermatitis; (2) demonstrate deleterious effects of passive smoking in nonsmokers with dermatological reactions; and (3) determine the cellular reaction occurring in the disorder, which is of unknown etiology.

Methods or Approach:

Familial dermatitis, resembling seborrhoeic dermatitis, was studied in patients with intracutaneous tests (tobacco leaf), passive cutaneous anaphylaxis (tobacco leaf, nicotine), radioallergosorbent test (tobacco leaf), and human basophil degranulation test (HBDT). HBDT was selected as a practical test to investigate new cases of seborrhoeic dermatitis with the hapten nicotine.

Results to Date:
In all patients, the HBDT gave positive results with either the allergen (tobacco) or the hapten (nicotine) bound to human serum albumin. There appears to be a cellular reaction to tobacco antigens and especially to nicotine in some patients. It is suggested that the human basophil degranulation test with nicotine might be used for the detection of an immediate hypersensitivity reaction.
Project Dates:
January 1981–January 1986.
Financial Support:
Laboratoire d'Allergologie.
Reference:
Sudan, B.J.L.; Sterboul, J. "Nicotine: An Hapten." (Letter). *British Journal of Dermatology* 104:349-350, 1981.

0248. SAINTE-MARGUERITE HOSPITAL, FACULTY OF MEDICINE, 270 Boulevard de Sainte-Marguerite, 13009 Marseille, France.

Project Title:
Longitudinal Study of the Means of Early Detection of Respiratory Illness in a Population of Bakers.

Principal Investigators:
Kleisbauer, J.P.
Objective:
To (1) evaluate the distribution of spirometric parameters in the population of bakers; (2) correlate the spirometric values with risk factors such as profession, tobacco use, and genetic factors; and (3) determine a better predictive test for lung disease by followup of the study population.
Methods or Approach:
Followup of 160 bakers will include questions on respiratory symptoms and lung diseases and a functional study with flow-volume curve, carbachol sensitivity, and N_2 washout. A total of 156 bakers have been studied, but results are not yet available.
Project Dates:
April 1981–1988.
Financial Support:
INSERM (810123); Institut d'Etudes et Recherches Pneumophtiocologiques; Securite Sociale.

0249. U.E.R. BIOMEDICALE DES SAINTE-PERES, 45 Rue des Saints-Peres, 75270 Paris, France.

Project Title:
Animal Models of Tobacco Dependence.

Principal Investigators:
Mo[illegible] R.; Le Houezec, J.; De Maio, A., et al.
Objective:
To investigate the possibility of obtaining a reproducible animal model of tobacco dependence in small animals (rat, mouse, hamster).
Methods or Approach:
Long-term intravenous infusions and self-administration by bar-pressing have been used.
Results to Date:
The nicotine self-administration models described in the literature have not been reproduced. Nicotine is aversive (taste-conditioned aversion) by i.p. and i.v. routes. Cocaine is also aversive, but in parallel experiments, self-injection in rats is rapidly obtained. The same results were not achieved with nicotine.
Future Plans:
Oral nicotine self-administration in rats will be attempted with portocaval anastomosis.
Financial Support:
Societe d'Etude de al Dependance Tabagique.

0250. INTERNATIONAL AGENCY FOR RESEARCH ON CANCER, 150 Cours Albert-Thomas, 69372 Lyon Cedex 08, France. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE FOR DISEASE PREVENTION, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Passive Smoking - Volume 9 in the IARC Series *Environmental Carcinogens: Selected Methods of Analysis.*

Principal Investigators:
O'Neill, I.; Hoffmann, D.; Brunnemann, K.
Objective:
To provide a set of body fluid, environmental, and sidestream smoke measuring methods that will allow the best assessment of exposure to passive smoking and the carcinogens contained therein.
Methods or Approach:
Detailed reviews will also be conducted on the nature of sidestream smoke, sampling techniques, and other aspects essential for resolving the present controversy on effects of passive smoking. A questionnaire will be used to review current epidemiological findings. An international review board (convened in December 1983) selected the methods and topics to be included and authors to be invited. The editorial board approved the outline. All manuscripts are subject to peer review and detailed editing assures clear and complete description of experimental procedures.
Results to Date:
Publication is expected in 1986.
Project Dates:
December 1983–1986.
Financial Support:
IARC; United Nations Environment Programme.

0251. AGIA SOPHIA CHILDREN'S HOSPITAL, INSTITUTE OF CHILD HEALTH, Goudi, Athens, Greece.

Project Title:
Smoking Behavior and Health Knowledge of Greek Adolescents in Athens.

Principal Investigator:
Kafatos, A.G.
Objective:
To study social and behavioral correlates of smoking in children; formulate ideas for effective preventive strategies early in life.
Methods or Approach:
Subjects were 1,113 students from 13 public schools randomly selected from three areas of Athens, representing different socioeconomic categories. Students had originally been examined in 1979, at 10 to 14 years of age. Two years later, 67 percent of the original participants were reexamined. All children were given a standardized self-administered questionnaire on smoking and health knowledge and data were collected on socioeconomic characteristics, physical activity, arterial blood pressure, and serum levels of lipids, vitamins, and minerals.
Results to Date:
Between 1979 and 1981, the proportion of daily cigarette smokers increased from 1.4 percent to 2.5 percent, while the proportion of occasional smokers decreased from 13.3 percent to 10 percent. It is possible that children that were reexamined in 1981 were not similar to the 1979 group because of self-selective sampling; children who could not be located had dropped out of school, and being less motivated, probably tended to smoke more. Daily or occasional smokers had first smoked at an average age of 12.1 years. Of the 657 reexamined, 158 (25 percent) reported having tried cigarettes. Daily smokers reported average consumption of 4.7 cigarettes/day. Among daily and occasional smokers, 24 percent reported inhaling deeply, 22 percent inhaled part of the smoke, 17 percent reported smoke reached only the pharynx, 10 percent inhaled only to the back of the mouth, and 25 percent let the smoke only enter the mouth. Nonfiltered cigarettes were smoked by 8.5 percent, 73 smoked filtered cigarettes, and 19 percent smoked any kind. Although 19 percent were uncertain, 76 percent were certain that they could discontinue smoking at any time. None of the students wanted to increase the number of cigarettes smoked, and 48 percent reported that they wanted to quit smoking. Among all students reexamined, 66 percent of fathers and 28 percent of mothers were smokers. These percentages were much higher for daily and occasional smokers. On health knowledge questions, 59 percent in 1979 and 65 percent in 1981 answered correctly (no significant change). The lack of health education in schools explains the lack of any significant improvement in health knowledge.
Financial Support:
Institute of Child Health, Greece; Health Department of Greece.
References:
(1) Kafatos, A.G.; Panagiotakopoulos, G.; Bastakis, N., et al. "Cardiovascular Risk Factor Status of Greek Adolescents in Athens." *Preventive Medicine* 10:173-186, 1981. (2) Kafatos, A.G.; Trakas, D.; Saraphidou, E., et al. "Smoking Among Children Aged 10-14 in Athens." *Iatriki* 40:373-379, 1091. (3) Wynder, E.L.; Williams, C.L.; Laakso, K., et al. "Screening for Risk Factors for Chronic Diseases in Children From Fifteen Countries." *Preventive Medicine* 10:121-132, 1981.

0252. EVANGELISMOS HOSPITAL MEDICAL CENTER, Department of Cardiology, 47 Vasilisis Sophias Avenue, Athens 140, Greece.

Project Title:
Cardiovascular Epidemiology in Greece.

Principal Investigator:
Aravanis, C.
Objective:
To determine the relationship between various risk factors and coronary heart disease among rural populations of Greece.
Methods or Approach:
This study is part of the research project concerning cardiovascular epidemiology among rural people on the islands of Crete and Corfu, Greece. It is concerned with time trends of the effect of smoking on the respiratory system in men 40 to 60 years of age, initially studied in 1960, who have been followed since. Subjects are men who live under stable conditions with regard to lifestyle, work, diet, and other habits. Evaluation includes physical examination, electrocardiograms at rest and after exercise, and testing for blood lipids and blood sugar. Dietetic studies are also conducted.
Results to Date:
Although there was a low prevalence and incidence of coronary heart disease found among Greek farmers, the rate was higher among smokers. Other risk factors were hypercholesteremia, sedentary lifestyle, and increasing age.
Project Dates:
September 1960–continuing.
Financial Support:
European Economic Community.

0253. UNIVERSITY OF ATHENS MEDICAL SCHOOL, Department of Hygiene and Epidemiology, 11527 Athens, Greece.

Project Title:
An Evaluation of the Effects of Legislation and Health Education on Tobacco Consumption in Greece.

Principal Investigator:
Vorgia-Dalla, P.
Objective:
To evaluate effects of legislation and health education on tobacco consumption in Greece compared with effects of similar activities in other countries of the European Economic Community.
Methods or Approach:
Time trends of tobacco consumption in association with the introduction of new legislation or health education measures will be evaluated.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1984–December 1985.
Financial Support:
University of Athens, Greece.

0254. UNIVERSITY OF ATHENS, Department of Hygiene and Epidemiology, Goudi 609, Athens, Greece.

Project Title:
Lung Cancer and Passive Smoking.

Principal Investigators:
Trichopoulos, D.; Kalandidi, A.; MacMahon, B.
Objective:
To study the possible consequences of passive smoking on lung cancer risk.
Methods or Approach:
A case-control study was conducted, comparing women with lung cancer with a control group. An extensive questionnaire was completed by cases and controls concerning demographic, socioeconomic, and other characteristics. Data on smoking habits of cases and controls and of their husbands were also collected.
Results to Date:
Data on 102 women with a final diagnosis of lung cancer other than adenocarcinoma or terminal bronchial carcinoma were compared with 251 controls; 77 of the cases and 225 of the controls were nonsmokers. The relative risk for a nonsmoker married to a smoker of < 1 pack/day was 2.4. Being married to a heavy smoker (≥ 21 cigarettes/day) carried a relative risk of 3.4, supporting the hypothesis that passive smoking is a risk factor for lung cancer.
Project Dates:
September 1978–1984.
Financial Support:
NCI (5PO1CA06373); Greek Ministry of Social Services.
References:
(1) Trichopoulos, D.; Kalandidi, A.; Sparros, L., et al. "Lung Cancer and Passive Smoking." *International Journal of Cancer* 27:1-4, 1981. (2) Trichopoulos, D.; Kalandidi, A.; Sparros, L. "Lung Cancer and Passive Smoking: Conclusion of Greek Study." (Letter). *Lancet* 2(8351):677-678, September 17, 1983. (3) Trichopoulos, D. "Passive Smoking and Lung Cancer." (Letter). *Lancet* 1(8378):684, March 24, 1984.

0255. UNIVERSITY OF ATHENS, MEDICAL SCHOOL, Department of Hygiene and Epidemiology, 11527 Athens, Greece.

Project Title:
Passive Smoking and Chronic Obstructive Lung Disease.

Principal Investigators:
Kalandidi, A.; Tzannes, S.; Trichopoulos, D.
Objective:
To conduct a comparative evaluation of active and passive smoking in etiology of chronic obstructive lung disease (COPD) among Greek women.
Methods or Approach:
A case-control study will be conducted with hospital controls (admitted for accidents) and general population control (friends of cases). A total of 100 cases and 150 controls from each group is targeted.
Results to Date:
Preliminary data show a clear association between COPD and active smoking and a suggestive association for passive smoking.
Project Dates:
January 1983–December 1985.
Financial Support:
University of Athens, Medical School; Greek Ministry of Health; Greek Cancer Society.

0256. UNIVERSITY OF ATHENS, Department of Hygiene and Epidemiology, Goudi 609, Athens, Greece. HARVARD SCHOOL OF PUBLIC HEALTH, Department of Epidemiology, 677 Huntington Avenue, Boston, Massachusetts 02115.

Project Title:
Passive Smoking, Air Pollution, and Diet in the Etiology of Lung Cancer.

Principal Investigators:
Trichopoulos, D.; MacMahon, B.; Kalandidi, A.
Objective:
To evaluate the relative roles of passive smoking, air pollution, and diet in the etiology of lung cancer among women who are not smokers.
Methods or Approach:
A case-control study will be conducted using both hospital and population controls.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–December 1987.
Financial Support:
Greek Ministry of Health; Greek Cancer Society.

0257. CANCER RESEARCH INSTITUTE, TOKYO, INSTITUTE OF RADIOLOGY AND ONCOLOGY, Division of Pathology, Tokyo, Japan. QUEEN ELIZABETH HOSPITAL, Kowloon, Hong Kong.

Project Title:
A Study of the Characteristics and Etiology of Lung Cancer in Chinese Females in Hong Kong.

Principal Investigators:
Ho, J.H.C.; Tsuchiya, E.; Tominaga, S., et al.
Objective:
To confirm previous findings on lung cancer risk factors in females; identify other as yet unidentified risk factors, especially among females who have never smoked.
Methods or Approach:
Histopathological diagnosis of bronchial carcinoma and its subtypes in Hong Kong Chinese women and Japanese female patients will be compared by joint review by pathologists in Hong Kong and Tokyo.
Results to Date:
Results are not yet available.
Project Dates:
April 1984–March 1986.
Financial Support:
Japanese Ministry of Education and Culture.

0258. UNIVERSITY OF HONG KONG, Medical Faculty, Department of Community Medicine, Hong Kong.

Project Title:
Cultural, Environmental, and Familial Backgrounds of Female Lung Cancer Patients in Hong Kong: A Retrospective Case–Control Study.

Principal Investigators:
Koo, L.C.; Ho, J.H.C.
Objective:
To identify environmental risk factors that contribute to the unusually high incidence rate of lung cancer among females in Hong Kong.
Methods or Approach:
Although approximately 95 percent of male lung cancer cases can be attributed to smoking, the smoking-related proportion among females was only 36 percent. Interviews were conducted with 200 female lung cancer patients and 200 neighborhood controls matched for age, socioeconomic status, and residence to determine history of exposure to various sources of carcinogens or bronchial irritants. Analysis for risk factors focused on passive smoking, cooking fuels, other air pollutants and inhalants, Chinese medicines, and dietary patterns.
Results to Date:
Passive smoking was not related to increased risk of lung cancer among nonsmokers; however, the possibility still exists that effects of passive smoking may be measurable only for some histological types that arise from specific locations in the lung. No consistent relationship was found between frequency and duration of exposure to different types of biomass fuels and lung cancer incidence. A dose–response relationship was found between symptoms of bronchial irritation (chronic phlegm and cough) and lung cancer in patients.
Future Plans:
To control for various confounding variables, conditional logistic regression analysis of the more than 350 variables is continuing. Monitoring of indoor air pollution levels and collection of urine for analysis of cotinine level are planned.
Project Dates:
June 1980–December 1986.
Financial Support:
University of Hong Kong; Hong Kong Anti-Cancer Society.

0259. UNIVERSITY OF HONG KONG, Department of Community Medicine, Li Shu Fan Building, 5 Sassoon Road, Hong Kong.

Project Title:
Lung Cancer in Chinese Women in Hong Kong - A Case–Control Study of Some Possible Causal Factors of Lung Cancer in Nonsmoking Women.

Principal Investigators:
Lam, T.; Kleevens, J.W.L.; Chan, W.C., et al.
Objective:
To (1) determine whether passive smoking is a causal factor in lung cancer among nonsmoking Chinese women; (2) establish relationship between passive smoking and histological types; and (3) study role of other factors such as cooking habits and residential, occupational, and dietary factors.
Methods or Approach:
Among 400 female patients with diagnosed primary lung cancer, structured questionnaires are used to obtain information on residential and occupational history, and exposure to dust and chemicals, fuel, and cooking oil. Patients are followed up and histologies are reviewed independently by at least two pathologists.
Results to Date:
Results are not yet available.
Project Dates:
1983–1985.
Financial Support:
University of Hong Kong.

0260. BUDAPEST BAJCSY-ZSILINSZKY HOSPITAL, TUBERCULOSIS INSTITUTE, X., Kobanyai ut 45, Budapest, Hungary.

Project Title:
Prospective Study to Determine High-Risk Groups for Lung Cancer.

Principal Investigator:
Abraham, E.

Objective:
To determine risk of lung cancer associated with varying smoking habits; assess any relationship between abnormal respiratory function values and/or respiratory damage and risk of lung cancer among smokers.

Methods or Approach:
Approximately 16,300 persons, all with negative x rays, completed a detailed questionnaire on their smoking habits. The questionnaire defined consumption, type of cigarette smoked (filtered vs. nonfiltered) and portion of the cigarette left unsmoked. Results of the respiratory screening were added to the questionnaire.

Results to Date:
After 3 years, the causal role of smoking in lung cancer etiology is emphasized. Subjects who were nonsmokers and had no other risk factors are considered risk free. Among heavy smokers, risk for lung cancer is not significantly different between men and women.

Project Dates:
1968–1985.

0261. SEMMELWEIS UNIVERSITY MEDICAL SCHOOL, First Department of Medicine, 2/a Koranyi Sandor Utca, H-1083 Budapest, Hungary.

Project Title:
Smoking and Involutional Bone Loss.

Principal Investigators:
Gergely, I.; Hollo, I.

Objective:
To determine whether tobacco smoking accelerates physiological bone loss during aging.

Methods or Approach:
Mineral content of the nondominant radius diaphysis of 149 healthy men and 234 healthy women, aged 60 to 79 years, was measured photon-absorptiometrically, using a Norland-Cameron MBA178 analyzer in a followup study.

Results to Date:
Bone mineral content of heavy smokers was found to be less than that of similar nonsmokers. Annual bone mineral loss was greater (i.e., involutional bone loss was more rapid) in smokers than in nonsmokers. Negative correlation was found between the estimated lifetime consumption of cigarettes and the actual amount of bone mineral. At under 70 years, annual mineral loss positively correlated with daily cigarette consumption. The role of altered body weight and height could be excluded from findings, suggesting that smoking directly affects bone metabolism. Findings indicate that smoking accelerates involutional bone loss, and thus should be considered as a risk factor that may contribute to onset of bone fractures and osteoporotic complaints.

Future Plans:
Osteoporosis morbidity and fracture incidence will be analyzed in smokers vs. nonsmokers at the end of a 10-year followup period.

Project Dates:
June 1976–January 1987.

Financial Support:
Semmelweis University Medical School.

0262. SEMMELWEIS UNIVERSITY DENTAL SCHOOL, Clinic of Conservative Dentistry, Mikszath Kalman ter 4, 1052 Budapest, Hungary.

Project Title:
Follow-Up Studies in Oral Leukoplakia.

Principal Investigator:
Banoczy, J.

Objective:
To define "high risk" for carcinoma in a followup group of oral leukoplakia patients by clinical, histological, and ultrastructural methods.

Methods or Approach:
During an observation period of 30 years the ratio of cancer-development will be observed, etiological factors (smoking, mechanical irritation, etc.) will be analyzed, and the histopathological and ultrastructural variables will be studied.

Results to Date:
The clinically erosive, histologically dysplastic group of oral leukoplakias seem to represent the "high risk" group. Smoking plays an important role in the development of oral leukoplakia: the majority of the followed-up oral leukoplakia patients were smokers.

Project Dates:
1957–1985.

Financial Support:
Semmelweis University.

References:
(1) Banoczy, J. *Oral Leukoplakia.* Boston, Martinus Nijhoff Publishers, 1982. (2) Banoczy, J. "Clinical and Histopathological Aspects of Premalignant Lesions." In: Van der Wall, J.; Snow, G.B. (Editors). *Oral Oncology.* Boston, Martinus Nijhoff Publishers, 1984, pp. 3-31.

0263. B.R.D. MEDICAL COLLEGE, Department of Social and Preventive Medicine, Gorakhpur, Uttar Pradesh, India.

Project Title:
A Study of Health Hazards of Smoking Amongst Medical Students of Various Medical Colleges of Northern India.

Principal Investigators:
Sandell, J.; Mehrotra, S.K.; Sati, T.R.

Objective:
To determine whether smoking is increasing among medical students in India, who form a large part of the community of medical and health personnel.

Methods or Approach:
A 50 percent random sample of all medical colleges of northern India are included in the study. Pretested questionnaires are mailed to all students (first through fifth year) in all selected colleges, distributed by wardens of hostels. Wardens are requested to return completed questionnaires.

Results to Date:
An earlier survey in Uttar Pradesh found that of 424 (26.5 percent) student smokers, 323 had definite signs and symptoms of harmful effects of smoking, such as cough (28.28 percent), throat irritation (19.70 percent), burning sensation in the abdomen (8.24 percent), and breathlessness (7.75 percent). Tachycardia and increased palpitation were common among smokers, and a good number of smokers suffered from ventilatory impairment. Many experienced headache and loss of appetite and 68.2 percent had a family history of smoking. It was evident that there was a progressive increase in the number of smokers and degree of smoking during college years.

Future Plans:
Based on study findings, recommendations will be made for a national program for control of smoking.

Project Dates:
January 1981–December 1985.

0264. CALCUTTA UNIVERSITY, UNIVERSITY COLLEGE OF SCIENCE, Department of Physiology, Electrophysiology Unit, 92 A.P.C. Road, Calcutta 700 009, India.

Project Title:
Role of Nicotine or Tobacco Smoke on Cardiovascular Function.

Principal Investigator:
Koley, J.

Objective:
To (1) investigate behavior and reactivity of different cardiac receptors and different baroreceptors and chemoreceptors during nicotine therapy and cigarette smoke inhalation; (2) study the effects of nicotine on cardiac muscle and its spontaneous contractile activity; and (3) investigate any correlation between changes in urinary bladder pressure and cardiovascular function produced by nicotine and cigarette smoke.

Methods or Approach:
Blood pressure (BP), urinary bladder pressure, respiration, and electrocardiograph are monitored by Beckman Dynograph in anesthetized monkeys and cats. Cardiovascular reflexes are studied by electrophysiological techniques. Receptors are located on the heart of open-chested artifically ventilated animals. Microelectrodes are used to record ganglionic transmission. Cardiac muscle contractions are recorded by isolated preparation and perfusion techniques.

Results to Date:
Intravenous nicotine injection initially reduced BP and heart rate (HR), followed by a rise in BP but no significant change in HR. Nicotine probably releases acetylcholine from vagal nerve endings in the heart, thereby depressing myocardial contractility, which results in lower BP and HR. The rise in BP is probably due to peripheral vasoconstriction produced by released catecholamine from peripheral sympathetic nerve endings by nicotine, supported by an increase in sympathetic nerve activity. Although the rise in BP coincided with increased urinary bladder pressure, they are not interdependent. The two functions are mediated by two different individual mechanisms; urinary bladder pressure is dependent on increased activity of purinergic nerve, causing release of purines that stimulate the P_2-receptor in the bladder. Nicotine may stimulate and inhibit spontaneous activities of heart muscle, depending on concentration administered.

Future Plans:
The following studies are in progress: (1) effects of nicotine on transmembrane potential of toad auricle and ventricle; and (2) effects of nicotine on neuronal activity of the stellate ganglion and preganglionic sympathetic nerve.

Project Dates:
January 1981–January 1986.

Financial Support:
Council of Scientific and Industrial Research, India (7/28/531/80-81/EMR-I).

0265. CALCUTTA UNIVERSITY, UNIVERSITY COLLEGE OF SCIENCE, Department of Physiology, Electrophysiology Unit, 92 A.P.C. Road, Calcutta 700 009, India.

Project Title:
Studies on the Respiratory Behaviour and Reactivities to Nicotine or Tobacco Smoking.

Principal Investigator:
Koley, J.

Objective:
To (1) observe whether pulmonary abnormalities resulting from tobacco smoke or nicotine are associated with excitation of different pulmonary receptors, including pulmonary J-receptors; (2) determine whether the irritant receptors are collapse receptors; and (3) investigate etiology of asthma associated with inhalation of cigarette smoke.

Methods or Approach:
Blood pressure, respiration, electrocardiograph, wedge pressure, and intrapleural pressure of anesthetized cats and monkeys are recorded on Beckman Dynograph. Effects of nicotine or tobacco smoke on lung stretch receptors, pulmonary J-receptors, intercostal motor neuron, and phrenic nerve activity are recorded by electrophysiological technique. Microelectrodes will be used to record effect of nicotine or tobacco smoke on activity of brain stem respiratory neurons.

Results to Date:
Intravenous injection of nicotine or inhalation of tobacco smoke in cats produces brief apnea followed by sustained hyperventilation, an effect that is resistant to atropine, physostigmine, phentolamine, and propranolol. Hexamethonium and guanethidine sulfate counteract nicotine-induced respiratory effects. Bilateral cervical vagotomy and desensitization of both

nodose ganglia by local application of xylocaine abolishes nicotine-induced apnea and hyperventilation. It is assumed that nicotine-induced respiratory changes are due to stimulation of autonomic nicotinic receptors or stimulation of pulmonary receptors.

Future Plans:
The following studies are in progress: (1) effects of nicotine on pulmonary J-receptors and nodose ganglion; and (2) brain stem respiratory neuronal activity and location of the site by histological techniques.

Project Dates:
September 1982–September 1985.

Financial Support:
MCR, India (45/98/82-BMS).

0266. CANCER RESEARCH INSTITUTE, CARCINOGENESIS DIVISION, Tata Memorial Centre, Parel, Bombay 400 012, India.

Project Title:
Studies on Tobacco Carcinogenesis.

Principal Investigators:
Bhide, S.V.; Nair, J.; Murdia, U.S.

Objective:
To analyze gaseous phases and smoke condensates from bidi, cigarettes, chutta, chillum, and hookah; study mutagenicity and carcinogenicity of tobacco smoke and its condensates.

Methods or Approach:
Smoke and smoke condensates of bidi, cigarette, and chillum will be analyzed for polycyclic aromatic hydrocarbons, volatile and tobacco specific nitrosamines, and HCN. Mutagenicity of smoke condensates will be tested using short term bacterial and mammalian test systems. Carcinogenicity will be tested in experimental animals.

Results to Date:
Smoke condensate from bidi has carcinogenic and promoter types of polycyclic aromatic hydrocarbons (in ng quantities) and hydrogen cyanide, carbon monoxide, and phenolic compounds. Smoke condensate from bidis and Indian cigarettes is mutagenic in the Ames test and in the micronuclei test in Swiss mice, and also induces mutations in V79 Chinese hamster cells.

Future Plans:
Smoke will be analyzed for nitrosamines and carcinogenicity will be tested in mice and hamsters.

Project Dates:
November 1982–December 1986.

Financial Support:
Cancer Research Institute, India.

0267. CENTRAL TOBACCO RESEARCH INSTITUTE, Rajahmundry, Andhra Pradesh 533 105, India.

Project Title:
Reduction of Tar and Nicotine in F.C.V. Tobacco by Post-Curing Processing.

Principal Investigators:
Kameswara Rao, B.V.; Murty, K.P.S.N.

Objective:
To reduce tar levels in tobacco leaf by a number of post-curing treatments.

Methods or Approach:
A bulk crop of tobacco (cv GSH$_1$) was grown during the 1982-1983 crop season and cured leaf of bright grades was collected. Bulk tobacco was divided into 1 kg lots and treated as follows: control, potassium citrate at three concentrations to increase leaf K percent to 3.4, 4.4, and 5.4 (from 2.4 percent); potassium ascorbate at three concentrations to increase leaf K percent to 3.4, 4.4, and 5.4; citric acid at three concentrations (1, 2, and 3 percent on leaf weight basis); ascorbic acid at three concentrations (1, 2, and 3 percent on leaf weight basis); and hydrogen peroxide at three concentrations (10, 20, and 30 percent). Solutions were applied in aqueous medium. Cigarettes were made from treated tobacco and the following observations were taken: smoke total particulate matter and nicotine and leaf analysis for potassium and nicotine.

Results to Date:
Results indicated that the highest reduction in TPM (35.2 percent) and nicotine (25.0 percent) was obtained with potassium citrate treatment, followed by hydrogen peroxide and potassium ascorbate. The higher the concentration of the additive the higher the reduction. Ascorbic acid produced no reduction in TPM and nicotine, indicating that potassium is responsible for reducing these smoke constituents. Citric acid treatment caused a slight reduction in TPM and nicotine, showing the superiority of potassium citrate. At the highest concentration of potassium citrate treatment, leaf potassium increased by about 300 percent (equivalent to 17.1 percent of potassium citrate added to tobacco). Leaf nicotine was substantially reduced by increased concentration of hydrogen peroxide, which agrees with results previously obtained. TPM from treated cigarettes will be subjected to mutagenicity test for evaluating the effect of potassium application on carcinogenic potential. Further attempts will be made to increase leaf potassium under field conditions to evaluate effect in TPM reduction.

Project Dates:
July 1983–July 1985.

Financial Support:
Central Tobacco Research Institute, India; Indian Council of Agricultural Research.

0268. CENTRAL TOBACCO RESEARCH INSTITUTE, Rajahmundry, Andhra Pradesh 533 105, India.

Project Title:
Chemical Studies on Lanka Tobacco and Its Smoke.

Principal Investigators:
Kameswara Rao, B.V.; Chakraborty, M.K.

Objective:
To determine chemical characteristics of lanka tobacco, an indigenous type grown in the delta islands of Krishna and Godavari (used locally for cheroots, cigars and snuff); document characteristics to help popularize export of this indigenous type of tobacco.

Methods or Approach:
Lanka tobacco powder was utilized for extraction of essential oils, alkaloids, petroleum ether soluble fractions, volatile and nonvolatile acids, carbonyls, and β-sitosterol glucoside. Cigarettes made of lanka tobacco were smoked and total particulate matter (TPM) was collected and analyzed for lipid constituents, semivolatiles, nonvolatiles, and hydroxybenzenes. Identification of individual compounds was performed by gas chromatography, gas chromatography/mass spectometry, high performance liquid chromatography, and infrared spectroscopy.

Results to Date:
Lanka tobacco leaf was thoroughly examined and constituents classified as essential oils, selected lipid consitituents, fatty acids, carbonyls, and phenolic substances. In addition to the lipid constituents, semivolatiles, nonvolatiles, and hydroxybenzenes in smoke TPM, alkaloids and related compounds found were nicotine, nornicotine, anatabine, myosmine, nicotine-1,

1'-dioxide, cotinine, N'-methyl anabasine, 2-2'-bipyridine, 3-3'-bipyridine, n-nitrosonornicotine, n-butanoyl nornicotine, and 4-vinyl pryidine. The proportion of the three primary alkaloids in fermented lanka tobacco was nicotine 97.1 percent, nornicotine 2.5 percent, and anabasine 0.3 percent. Fermentation resulted in a reduction of 36.9 percent in total alkaloids. Individually, losses of nicotine, nornicotine, and anabasine during fermentation were 34.9 percent, 20.0 percent, and 66.6 percent, respectively. Alkaloids in the semivolatile phase were nicotine, myosmine, and nicotyrine, which are found in tobacco leaf also, thus indicating direct transfer to smoke. Quantitatively, the transfer rate of nicotine to TPM was 17.5 percent. It is significant that no nornicotine was found in smoke TPM. In the phenolic acid fraction, five nonvolatile acids were identified; fumaric, malonic, maleic, citric, and succinic. Phenolic acids assume significance owing to their possible role as precursors of tumorigenic catechols and phenols in smoke. It is significant that the research cigarette and lanka cigarette smoke were found to have similar phenol concentration, since phenols play a contributory role in tumor formation and in toxicity of tobacco smoke in ciliated epithelium.

Project Dates:
June 1978–July 1983.

Financial Support:
Central Tobacco Research Institute, India; Indian Council of Agricultural Research.

0269. GUJARAT CANCER AND RESEARCH CENTER, NCH Campus, Asarwa, Ahmedabad, Gujarat 380 016, India.

Project Title:
Study of Incidence of Cancer in Women Using Tobacco as Snuff Powder for Inhalation Through Nose and Using Snuff Powder for Cleaning of Teeth in Certain Areas of Gujarat State.

Principal Investigators:
Patel, T.B.; Balar, D.B.; Patel, R.D.

Objective:
To investigate the history of oropharyngeal, lung, and esophageal cancer in women admitted to the hospital of the Gujarat Cancer and Research Institute.

Methods or Approach:
In 1983, women accounted for 2,463 of the 6,620 new cancer cases admitted to the center's 400-bed hospital. For each case, a full history was taken including age, occupation, personal habits, socioeconomic status, area of residence, and cultural habits such as using tobacco powder for cleaning teeth.

Results to Date:
Preliminary findings show that of female cancer cases admitted during 1983, 15.2 percent were oropharyngeal, 5.6 percent esophageal, 1.6 percent lung, and 0.8 percent laryngeal.

Project Dates:
November 1984–November 1986.

Financial Support:
Gujarat State Government; Government of India.

0270. GUJARAT CANCER AND RESEARCH INSTITUTE, New Civil Hospital Campus, Asarwa, Ahmedabad, Gujarat 380 016, India.

Project Title:
Role of Tobacco in the Causation of Cancer in the Industrial Workers of Ahmedabad Corporation Complex (Gujarat State).

Principal Investigators:
Patel, T.B.; Patel, D.D.; Rajani, S.P.C.

Objective:
To determine the role of tobacco consumption in the development of cancer among the industrial workers of the Ahmedabad Corporation Complex.

Methods or Approach:
The complex has a male population of 1,223,253, and includes 124,714 industrial workers in 119 textile mills and industries, the highest number in the State of Gujarat. There are also 511,256 male nonindustrial workers over the age of 20. By analyzing the cancer cases admitted to the Gujarat Cancer and Research Institute's cancer hospital, the cancer incidence among the industrial workers and in the nonindustrial population will be determined and compared with the incidence in other districts of the State, to ascertain the role of tobacco consumption in the etiology of cancer in the industrial population.

Results to Date:
Results so far suggest that while industrial workers are exposed to environmental and occupational hazards, the use of tobacco, particularly the practice of bidi smoking, is a significant risk factor for the development of cancer. Among the 124,714 industrial workers there were 1,261 reported cases of cancer, a rate almost twice that in the general population. A higher percentage of the workers were smokers: 69 percent compared with 55 percent of the cancer patients from the general population, while male smokers in the general population over 20 years of age constituted only 44 percent.

Project Dates:
April 1982–1987.

Financial Support:
Gujarat Cancer and Research Institute; Ministry of Health, India.

0271. GUJARAT CANCER AND RESEARCH INSTITUTE, NCH Campus, Asarwa, Ahmedabad, Gujarat 380 016, India.

Project Title:
Study of Incidence of Cancer in the Tobacco Smoking Community and Investigation of Its Effect in Causing Differential High Incidence of Cancer in Certain Sites.

Principal Investigators:
Patel, T.B.; Patel, R.D.; Patel, D.D.

Objective:
To study the incidence of cancer caused by smoking bidis (indigenous cigarettes) in Gujarat State compared with western countries.

Methods or Approach:
In 1983, 6,620 new cancer cases (confirmed by clinical, radiological, and pathological examinations) were admitted to the 400-bed clinic hospital. To carry out case studies of oropharyngeal, laryngeal, and lung cancer, information was obtained on smoking habits, including manner of smoking, number of cigarettes or bidis smoked/day, and whether tobacco (or tobacco pan and lime) was chewed.

Results to Date:
In western countries, cigarette smoking is associated with the high incidence of lung cancer. In Gujarat State, where bidis are commonly smoked by people in rural areas and among poor or lower middle class groups in urban areas, there is not only a high incidence of lung cancer, but also oropharyngeal and laryngeal cancer. In males, 47.5 percent of all cancer cases observed at the cancer institute were oral, pharyngeal, or laryngeal compared with 17 percent in the United States and

8.3 percent in Australia. For lung cancer, the rates were 12.1 percent of total male cancer cases in Gujarat State, 62.4 percent in the United States, and 47.5 percent in Australia. Reasons for such differences may be (1) the way cigarettes are smoked (deep inhalation is not common in Gujarat State); (2) bidis are wrapped in tobacco leaf rather than paper; and (3) the quantity of tar, nicotine, and other products inhaled may be of different proportions. Alcohol consumption, which may have synergistic or supplemental effects with smoking, is prohibited in Gujarat State (although there may be some clandestine drinking).

Project Dates:
November 1984–November 1986.

Financial Support:
Gujarat State Government (India); Government of India.

0272. GUJARAT CANCER AND RESEARCH INSTITUTE, New Civil Hospital Compound, Ahmedabad, Gujarat 380 016, India.

Project Title:
Cytogenetic Studies in Individuals Chewing Tobacco.

Principal Investigator:
Adhvaryu, S.G.

Objective:
To study the relationship between chewing tobacco and development of oral cancer; determine parameters that may prove useful in identifying individuals prone to tobacco-induced genomic damage.

Methods or Approach:
Cytogenetic parameters to be studied include spontaneous and mutagen-induced sister chromatid exchange frequencies, chromosome aberrations, and C-band polymorphism rates. Subjects will include normal healthy individuals who do not consume tobacco in any form; individuals who have chewed tobacco for at least the past 2 years, but who are without alterations in morphology of oral mucosa; and tobacco chewers with oral submucus fibrosis/leukoplakia. Peripheral blood lymphocytes will be the source of experimental material. It is anticipated that there will be approximately 50 subjects in each group.

Results to Date:
Project is in a preliminary phase.

Project Dates:
April 1984–March 1987.

Financial Support:
Gujarat Cancer and Research Institute, India.

0273. KURUKSHETRA UNIVERSITY, Department of Physics, Kurukshetra 132 119, India.

Project Title:
Study of Trace Amount of Uranium in Snuff.

Principal Investigators:
Sharma, P.K.; Lal, N.; Nagpaul, K.K.

Objective:
To determine role of radioactivity in cancer risk among snuff users by measuring uranium concentration in snuff.

Methods or Approach:
Fission track etch technique was used to measure uranium content. After sandwiching between thoroughly washed lexan detectors, pellets of snuff and uranium standard (glass) were irradiated in thermal column of CIBUS reactor at Bombay. Lexan detectors were etched and tracks counted. To calculate uranium in snuff, track density of snuff pellet detectors was compared with uranium standard pellet.

Results to Date:
Uranium activity in snuff varied from 2.4 to 6.4 pCi/g (mean 3.7 pCi/g), which is very high compared with uranium content in cigarette tobacco. Results suggest that the main contribution of activity in snuff comes from ingredients other than tobacco.

Project Dates:
August 1983–January 1984.

Financial Support:
Government of India, Department of Atomic Energy.

0274. MAULANA AZAD MEDICAL COLLEGE, New Delhi, India. G.P. PANT HOSPITALS, New Delhi, India.

Project Title:
In Vitro Study of Cell Mediated Immunity Against Tobacco in Patients With Thromboangiitis Obliterans (TAO).

Principal Investigator:
Gulati, S.M.

Objective:
To investigate possible role of tobacco antigen in thromboangiitis obliterans (TAO).

Methods or Approach:
Leukocyte migration inhibition and lymphocyte trasfuration tests were employed to test in vitro cell mediated immunity against tobacco and specific human arterial homogenate extracts.

Results to Date:
TAO patients showed specific inhibition of migration of leukocytes against arterial and tobacco antigens compared with a control group. A statistically significant difference was observed in mean migration index of patients against arterial antigen ($p<0.001$) and tobacco antigen ($p<0.01$). In addition, lymphocytes from patients showed greater H^3-thymidine uptake against arterial and tobacco antigens compared with healthy controls; however, the difference in mean stimulation indices between the two groups was not statistically significant.

Project Dates:
January 1970-July 1982.

Financial Support:
Indian Council of Medical Research.

0275. POSTGRADUATE INSTITUTE OF MEDICAL EDUCATION AND RESEARCH, Department of Chest Diseases, Chandigarh 160 012, India.

Project Title:
Tobacco Smoking and Other Background Variables in Chronic Cor Pulmonale.

Principal Investigators:
Jindal, S.K.; Malik, S.K.

Objective:
To investigate the role of smoking, especially bidi and hukka, in the development of chronic cor pulmonale in India in relation to other factors such as occupation, housing, and other living conditions.

Methods or Approach:
Patients diagnosed as chronic cor pulmonale are studied. Details of smoking history, residence, and other personal factors are recorded; and the status of cardiorespiratory function is determined. Any other possible underlying illness is also investigated.

Results to Date:
Of the 307 patients diagnosed during the past 5 years, 179 were smokers, with differences noted by sex and age. The smoker–nonsmoker ratio was 0.9:1.0 for the youngest age groups, but

rose to 1.9:1.0 in the oldest. An equal number smoked cigarettes and bidis; fewer smoked hukka. Smoking habits differed more according to religion than by place of residence.

Future Plans:

A larger number of patients will be studied, and the etiological factors in nonsmokers will be carefully examined, especially the role of allergy and the influence of smoke from domestic fuels.

Project Dates:

January 1981–1983.

Financial Support:

Postgraduate Institute of Medical Education and Research, India.

0276. POSTGRADUATE INSTITUTE OF MEDICAL EDUCATION AND RESEARCH, Department of Chest Diseases, Chandigarh 160 012, India.

Project Title:

Reverse Smoking and Chronic Obstructive Lung Disease.

Principal Investigators:

Malik, S.K.; Behera, D.; Jindal, S.K.

Objective:

To determine the frequency of symptoms of chronic respiratory disease and changes in lung functions associated with "chutta" smoking in India.

Methods or Approach:

Reverse smoking (keeping the lighted end inside the mouth) is a popular and peculiar habit prevalent among the adults of the southeastern coastal towns and villages of India. A few dried twigs of homegrown tobacco are rolled crudely in a semidried tobacco leaf. The finished product is called chutta. Chutta smokers living in the coastal area of Orissa (mostly fishermen and laborers) are being studied. Respiratory symptoms are evaluated with the help of a standard questionnaire. Peak expiratory flow rate is recorded on a Wright peak flow meter and FEV_1 is measured directly on a battery-operated portable minispirometer.

Results to Date:

Adults in the coastal village of Gopalpur, Orissa (n=258), were examined. Of these, 72 females and 41 males were pure chutta smokers; 59 were nonsmokers; the rest were mixed smokers. Chronic bronchitis with or without airways obstruction was diagnosed in 37 cases (32.7 percent). Details are being evaluated.

Future Plans:

A larger number of subjects will be studied to evaluate the changes in pulmonary function tests.

Project Dates:

July 1981–December 1982.

Financial Support:

Postgraduate Institute of Medical Education and Research, India.

0277. POSTGRADUATE INSTITUTE OF MEDICAL EDUCATION AND RESEARCH, Department of Chest Diseases, Chandigarh 160 012, India.

Project Title:

Effects of Tobacco Smoking on Airway Reactivity to Inhaled Bronchoconstrictor - Methacholine.

Principal Investigators:

Jindal, S.K.; Malik, S.K.; Kashyap, S., et al.

Objective:

To (1) determine airway responsiveness to methacholine aerosol in apparently healthy persons (nonsmokers, asymptomatic smokers, and symptomatic smokers) (2) establish relationship of airway response to different kinds of smoking, degree and duration of smoking, and to airway obstruction.

Methods or Approach:

Aerosolized methacholine is administered in doubling doses to subjects who inhale the agent from a Wright nebulizer for 2 min of tidal breathing. A maximum of 11 doses is given, starting with 0.031 mg/mL. Measurement of peak expiratory flow rate and forced expiratory volume in 1 sec (FEV_1) are repeated after every dose. Tests are discontinued after a dose at which FEV_1 falls by 20 percent from mean baseline value.

Results to Date:

Project is in a preliminary phase.

Future Plans:

Alterations in airway response will be studied in smokers vs. nonsmokers and in asymptomatic smokers vs. symptomatic smokers and smokers with chronic bronchitis and emphysema.

Project Dates:

April 1984–March 1986.

Financial Support:

Postgraduate Institute of Medical Education and Research, India.

0278. POSTGRADUATE INSTITUTE OF MEDICAL EDUCATION AND RESEARCH, Department of Chest Diseases, Sector 12, Chandigarh (Union Territory) 160 012, India.

Project Title:

Chemistry of Tobacco Smoke in Chutta - A Home Made Cigar.

Principal Investigators:

Malik, S.K.; Behera, D.

Objective:

To examine the chemistry of tobacco smoke produced by home-made cigars that are popular in Orissa State (southeast India).

Methods or Approach:

Chemical analysis was carried out by standard techniques. Analysis of tobacco smoke was carried out on smoking machine SM-I. Chutta tobacco was analyzed for percentage of reducing sugars, nicotine, alkaloids, chloride, and total nitrogen (in collaboration with the Central Tobacco Research Institute, Rajahmundry, India).

Results to Date:

The chutta tobacco analyzed contained 1.41 percent nicotine, 1.10 percent reducing sugars, 1.30 percent chloride, and 2.95 percent total nitrogen. A large chutta (length 98 mm, mean weight 2,843 mg) had a mean dry total particulate matter of 115.1 mg; mean nicotine content was 8.125 mg. Values for a small chutta (length 73 mm, weight 1,291 mg) were 60.6 mg and 4.625 mg, respectively. Average pH range of chutta smoke was 7.6 to 7.8. Temperatures recorded during burning were 240° C during quiet burning, 300° C during normal puffing, and 360° C at maximum puffing (normal smoking).

Financial Support:

Postgraduate Institute of Medical Education and Research, India.

0279. POSTGRADUATE INSTITUTE OF MEDICAL EDUCATION AND RESEARCH, Department of Chest Diseases, Chandigarh (Union Territory) 160 012, India.

Project Title:
Effect of Long-Term Tobacco Smoking: Spirometric Evaluation in Males Aged More Than 55 Years.

Principal Investigators:
Malik, S.K.; Dhand, R.
Objective:
To conduct simple spirometry on subjects over the age of 55 who smoke.
Methods or Approach:
Measurements made included forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV_1), FEV_1/FVC ratio, forced expiratory flow at 25 to 75 percent (FEF_{25-75}), and forced expiratory time for 50 percent vital capacity (FET_{50}) and 80 percent vital capacity (FET_{80}). A total of 150 male smokers over the age of 55 years and an equal number of age-matched nonsmokers (controls) were studied.
Results to Date:
Symptoms of chronic bronchitis and changes in FEV_1, FEF_{25-75}, and FET_{50} were significantly more abnormal among smokers, with a direct correlation with amount smoked. Subjects with normal FEV_1/FVC ratio (>70 percent) had no demonstrative change in FEF_{25-75} and FET_{50}. However, smokers with symptoms (but with normal FEV_1/FVC ratio) showed prolongation of FET_{50}. It is concluded that a simple test like FEV_1 is highly discriminatory for evaluating lung function changes in smokers.
Project Dates:
1984–1984.
Financial Support:
Postgraduate Institute of Medical Education and Research, India.

0280. POSTGRADUATE INSTITUTE OF MEDICAL EDUCATION AND RESEARCH, Department of Chest Diseases, Chandigarh (Union Territory) 160 012, India.

Project Title:
Role of Passive Smoking in the Genesis of Chronic Respiratory Disease in Women.

Principal Investigators:
Malik, S.K.; Gilhotra, R.S.
Objective:
To examine the role of active tobacco smoking by male members of a family on the health status of spouses (and children).
Methods or Approach:
House-to-house visits will be conducted; selected sample will be matched for age and economic status. Only urban residents will be screened initially. Questionnaires will be used to record history of respiratory disease. Peak expiratory flow and forced expiratory volume in 1 sec will be monitored. Urine samples will be analyzed for nicotine at a later stage of the project.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–December 1985.
Financial Support:
Postgraduate Institute of Medical Education and Research, India.

0281. POSTGRADUATE INSTITUTE OF MEDICAL EDUCATION AND RESEARCH, Department of Chest Diseases, Chandigarh 160 012, India.

Project Title:
Chronic Bronchitis and Respiratory Function Impairment in Chutta Smokers (Reverse Smoking).

Principal Investigators:
Behera, D.; Malik, S.K.
Objective:
To study prevalence of chronic respiratory disease in reverse smokers.
Methods or Approach:
Personal interviews, utilizing standard questionnaires, were used in the cross-sectional study of available population. A total of 374 subjects was examined and their respiratory symptoms were evaluated. Peak expiratory flow rate (PEFR) or forced expiratory volume in 1 sec (FEV_1) were measured by portable meters.
Results to Date:
Of the 374 persons examined, 225 (51 males and 174 females) were reverse chutta smokers. Overall frequency of chronic bronchitis, according to duration of smoking, was 0.0 percent in those who had smoked for 1 to 10 years, 13.5 percent for 11 to 20 years; 13.5 percent for 21 to 30 years; 24.0 percent for 31 to 40 years; and 49.0 percent in those who had smoked for over 40 years. Reverse smokers had lower values of PEFR and FEV_1 than nonsmokers, and values were significantly reduced in symptomatic subjects of both sexes ($p < 0.01$).
Project Dates:
1982–Continuing.
Financial Support:
Postgraduate Institute of Medical Education and Research, India.
Reference:
Malik, S.K.; Behera, D.; Kindal, S.K. "Reverse Smoking and Chronic Obstructive Lung Disease." *British Journal of Diseases of the Chest* 77(2):199-201, 1983.

0282. POSTGRADUATE INSTITUTE OF MEDICAL EDUCATION AND RESEARCH, Department of Pharmacology, Chandigarh 160 012, India.

Project Title:
Drug Metabolizing Studies With Tolbutamide.

Principal Investigators:
Sharma, P.L.; Uppal, R.
Objective:
To study effect of chronic cigarette smoking on tolbutamide kinetics.
Methods or Approach:
Tolbutamide kinetics were studied in normal nonsmoking volunteers who had smoked for periods of 4 to 20 years. Tolbutamide (500 mg) was administered after an overnight fast, and serial samples of blood were collected for 10 hours. Plasma was separated and concentration of tolbutamide was estimated.
Results to Date:
Although the half-life of tolbutamide was reduced in smokers (5.69 ± 1.94 vs. 8.27 ± 3.55 hours, $p > 0.05$), the difference was not significant. However, reduction in area under the time concentration curve and peak concentration were significant ($p < 0.001$ and $p < 0.05$, respectively), demonstrating that cigarette smoking enhances metabolism of tolbutamide.
Project Dates:
April 1981–May 1983.

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Financial Support:
Postgraduate Institute of Medical Education and Research, India; MRC, India.

0283. RURAL HEALTH CENTER, PODAD, P.O. Gudibanda 508 206, India.

Project Title:
Fear of God - Religious Restrictions: Effective Tool for Control of Smoking and Ultimate Stoppage.

Principal Investigators:
Prasad, V.H.; Rao, S.A.; Prasad, K.S.R., et al.

Objective:
To determine whether religious affiliation and strict religious restrictions could be used as a tool for smoking cessation; determine whether smoking could be controlled by exploiting the religious sentiments in theists.

Methods or Approach:
People were made to believe (by passing on religious facts) that a visit to Swami Ayyapra in Babarmalai would confer divinity, peace, and prosperity. However, one should lead a pious life (including no drinking or smoking) for about 60 days before visiting the temple. People were told to abstain from smoking completely, without even thinking of cigarettes, and that any violation of this rule would result in severe punishment by God.

Results to Date:
A total of 549 people who were smoking ≥ 40 cigarettes or bidis/day were able to stop abruptly from the day they took an oath to visit the Diety. The fear of God and the desire to get good results out of the pilgrimage helped them develop self-control and the will power to resist temptation. All were successful for the 60 days, 50 percent remained abstinent for 2 to 3 years, and 30 percent were still abstinent after more than 5 years.

Future Plans:
Observations of the group will be continued for 10 years and other smokers will be recruited into the Ayyapra cult to promote cessation of smoking.

Project Dates:
October 1979–1989.

0284. S.M.S. MEDICAL COLLEGE AND HOSPITAL, Upgraded Department of Medicine, Jaipur, Rajasthan 302 004, India.

Project Title:
Effect of Tobacco Consumption on Diabetic Retinopathy.

Principal Investigators:
Khandelwal, P.D.; Bhu, N.; Khandelwal, S., et al.

Objective:
To determine effect of smoking, tobacco consumption, and other factors on diabetic retinopathy.

Methods or Approach:
Diagnosis, based on clinical history, examination, and laboratory findings, was made in 100 diabetic patients presenting with gradual loss of vision and other symptoms suggestive of diabetes mellitus. Of these, 62 had nonproliferative and 38 had proliferative retinopathy (area of fluorescein leak characteristic of neovascularization). Tobacco consumers were regular smokers or regular chewers of tobacco (betel or any other form) for 7 years prior to the study. There were 58 consumers and 42 nonconsumers. Nonsmokers were patients who had not smoked for at least 7 years prior to the study. Patients were grouped by consumption level.

Results to Date:
Increasing tobacco consumption was significantly associated with proliferative retinopathy, and directly related to amount of tobacco used or number of cigarettes smoked. Increase in proliferative retinopathy was found to be associated with both duration of diabetes and amount of tobacco used. Control of diabetes had no significant influence on progress of retinopathy or any effect in making it less severe.

Future Plans:
Effect of tobacco consumption and cigarette smoking on diabetic nephropathy will be observed.

Reference:
Khandelwal, P.D.; Bhu, N.; Khandelwal, S., et al. "Effect of Tobacco Consumption on Diabetic Retinopathy." *Journal of Association of Physicians of India* 30(9):609-611, September 1982.

0285. S.M.S. MEDICAL COLLEGE, Upgraded Department of Medicine, Jaipur, Rajasthan 302 004, India.

Project Title:
Comparative Analysis of the Effects of Cigarette Smoking and Tobacco Chewing on Serum HDL Cholesterol.

Principal Investigators:
Khandelwal, P.D.; Narula, J.; Khandelwal, S., et al.

Objective:
To elucidate and compare effects of cigarette smoking and tobacco chewing on serum high density lipoprotein cholesterol (HDL-C) status, and thus on coronary atherosclerosis.

Methods or Approach:
Subjects were 120 randomly selected men; 40 current nonsmokers/nonchewers (21 never smokers/chewers, 19 ex-smokers/chewers), 40 current smokers, and 40 current chewers. Factors that alter HDL-C status (and obscure findings) were avoided, including diabetes, hypertension, obesity, and endocrinometabolic and renal disorders. Data on alcohol consumption and regular exercise were obtained. Subjects were not consuming any lipid-lowering drugs or beta blockers, and were considered to have been eating an average diet. HDL-C was obtained by enzymatic colorimetric CHOD-PAP method.

Results to Date:
HDL-C levels were significantly low in light, moderate, and heavy smokers. Although light tobacco chewing did not have any impact on HDL, moderate to heavy chewing significantly decreased HDL. Ex-smokers and ex-chewers have almost normal HDL values. Moderate alcohol consumption and regular jogging did not have any impact on HDL. It is proposed that cigarette smoking (in any amount) and tobacco chewing in moderate to heavy quantities significantly decrease HDL-C levels, but that levels can be reversed by quitting. A dose–response relationship was discerned.

0286. TATA INSTITUTE OF FUNDAMENTAL RESEARCH, Basic Dental Research Unit, Homi Bhabha Road, Bombay 400 005, India.

Project Title:
Oral Cancer and Precancerous Conditions in Rural Indian Populations.

Principal Investigators:
Mehta, F.S.; Gupta, P.C.

Objective:
To elucidate the natural history of oral precancerous lesions and their association with tobacco habits.

Methods or Approach:
Oral cancer is the most common form of cancer in India. It is

said to be frequently preceded by white lesions considered precancerous. About 100,000 individuals residing in Ambegaon and Junnar Taluks of Poona district were examined for the presence of oral precancerous lesions and tobacco habits. The individuals with lesions along with suitable matched controls are now being followed up annually. They are also being subjected to intervention measures to encourage them to give up their tobacco habits, by personal communication, films, posters, radio programs, and newspaper articles.

Results to Date:
Study data are being analyzed.

Project Dates:
September 1975–1986.

Financial Support:
NCI (01-22-N).

0287. TATA INSTITUTE OF FUNDAMENTAL RESEARCH, **Basic Dental Research Unit, Homi Bhabha Road, Bombay 400 005, India.**

Project Title:
Effect of Intervention on Mortality Experience Among Tobacco Users.

Principal Investigators:
Gupta, P.C.; Mehta, F.S.

Objective:
To determine whether there is any reduction in the mortality among tobacco users when tobacco habits are either discontinued or reduced significantly.

Methods or Approach:
Samples of 12,000 tobacco users have been interviewed in rural areas of Ernakulam district, Kerala State, Srikakulam district, Andhra Pradesh, and Bhavnagar district, Gujarat State. The villagers are being exposed to a concentrated program of education, motivation, and guidance to persuade them to give up their tobacco habits. All the individuals are reinterviewed annually. A significant reduction in a tobacco habit is defined as 50 percent or more reduction in the frequency of tobacco use. For individuals who smoke as well as chew tobacco, significant reduction includes discontinuation of one habit without increasing the frequency of the other. A person is placed in the "discontinued" category if tobacco has not been used in any form during the preceding 6 months. The method of person-years is being used for the data analysis. The mortality rates will be adjusted with respect to age and sex.

Results to Date:
Project is still in the data collection stage.

Project Dates:
July 1978–1986.

Financial Support:
Tata Institute of Fundamental Research.

0288. TATA INSTITUTE OF FUNDAMENTAL RESEARCH, **Basic Dental Research Unit, Homi Bhabha Road, Bombay 400 005, India.** ROYAL DENTAL COLLEGE, **Department of Oral Pathology, 4 Universitetsparken, Copenhagen, Denmark.**

Project Title:
Intervention Study of Oral Cancer and Precancerous Lesions in Relation to Tobacco Use in Rural Indian Populations.

Principal Investigators:
Mehta, F.S.; Pindborg, J.J.

Objective:
To determine whether the association between precancerous lesions, oral cancer, and tobacco habits is direct by demonstrating a reduction in the incidence of precancerous lesions when tobacco habits are discontinued.

Methods or Approach:
A sample of 12,000 individuals with tobacco habits has been examined and interviewed in each of the three rural areas under study. The villagers are being persuaded to give up their tobacco habits by exposure to a concentrated program of education, motivation, and guidance. The villagers are being shown a documentary film, and impact studies of the film will be conducted in each of the three areas. The message will also be communicated to each of the examined individuals. In addition, the population is being subjected to visual, audio, and other media support. Currently, these include placement of handwritten and pictorially printed posters on prominent sites; radio broadcasts of plays, talks, and interviews; personal communication through a social scientist; newspaper articles; and folk dramas. These individuals are being reexamined annually to assess changes in tobacco habits, development of new oral precancerous lesions, and changes in previously diagnosed lesions.

Results to Date:
The results from the first followup revealed that 3-5 percent of the individuals stopped practicing their tobacco habits in different areas and 1-16 percent reduced their tobacco habits. The regression rate of leukoplakia among those who stopped or reduced their tobacco habits was four to seven times higher in different areas compared to those who did not change their tobacco habits. The difference was statistically significant for all the three areas.

Future Plans:
The annual followup will be continued. Strategies for intervention will be revised on the basis of feedback studies. Apart from the evaluation of the overall impact, each medium of intervention will also be evaluated separately.

Project Dates:
July 1978–1986.

Financial Support:
NCI (01-022-N).

0289. TATA INSTITUTE OF FUNDAMENTAL RESEARCH, **Basic Dental Research Unit, Homi Bhabha Road, Bombay 400 005, India.**

Project Title:
Mortality Rates Among Different Tobacco Habit Groups in a Rural Indian Population.

Principal Investigators:
Gupta, P.C.; Mehta, F.S.

Objective:
To compare the mortality rates among bidi smokers, tobacco chewers, those who practice both kinds of tobacco habits, and those who do not practice any kind of tobacco habit.

Methods or Approach:
During 1967-1968, information on tobacco habits was collected from a random sample of 30,000 adult individuals in the Bhavnagar, Ernakulam, and Srikakulam districts in India. For the next 10 years, information regarding mortality among these individuals was collected as a part of a larger house-to-house survey. Information regarding mortality was collected for 8 years in Pune district for about 1,300 oral lesion cases practicing different kinds of tobacco habits and matched controls. These data are being used to compute the mortality rates for different tobacco habit groups using the method of person-years.

Results to Date:
The data from Pune district reveal a significantly higher death

rate among bidi smokers than among tobacco chewers. The study was completed and results were published.

Project Dates:
July 1978–1981.

Financial Support:
Tata Institute of Fundamental Research.

References:
(1) Gupta, P.C.; Mehta, F.S. "Mortality Experience in Relation to Tobacco Chewing and Smoking Habits From a 10-Year Follow-Up Study in Ernakulam District, Kerala." *International Journal of Epidemiology* 13:184-187, 1984. (2) Gupta, P.C.; Mehta, F.S. "Mortality Among Reverse Chutta Smokers in South India." *British Medical Journal* 289(6449):865-866, 1984.

0290. TATA INSTITUTE OF FUNDAMENTAL RESEARCH, **Basic Dental Research Unit, Homi Bhabha Road, Bombay 400 005, India.**

Project Title:
Investigation of Causes of Mortality Among Tobacco Users in Rural Indian Populations.

Principal Investigators:
Gupta, P.C.; Mehta, F.S.

Objective:
To determine the possible causes of mortality among tobacco users (bidi smokers, chukka smokers, reverse chukka smokers, and tobacco chewers) in rural Indian populations.

Methods or Approach:
The causes of mortality among cigarette smokers have been studied and reported in great detail in the literature. In India, tobacco is smoked in the form of bidi, chukka, and reverse chukka smoking (a homemade cheroot, with burning end inside the mouth). Tobacco is used for chewing also. In rural India where these habits are very common, it is difficult to ascertain the cause of death. The patients may not be seen by any qualified medical person before death nor admitted to any hospital. Even with hospital admission, it is quite difficult to determine the medical history due to the poor medical records system in interior rural hospitals. In the present study the approach is to collect information from family members on the symptoms exhibited by the person just before the death. Samples of 12,000 tobacco users are being interviewed annually in the rural areas of Ernakulam district (Kerala) and Srikakulam district (Andhra Pradesh) for this purpose. In the same villages, individuals who do not use tobacco in any form are used as controls. A special checklist questionnnaire containing an exhaustive listing of possible symptoms before death has been prepared and pretested. The symptoms are noted irrespective of the information available about the cause of death. The interviews will be conducted annually so that, in general, the time interval between death and questionnaire interview will remain at less than a year.

Results to Date:
It appears that for older individuals (60 years and over) it may be somewhat difficult to establish a cause of death. For younger individuals (less than 50 years), however, the study may provide useful information.

Project Dates:
July 1978–1986.

Financial Support:
Tata Institute of Fundamental Research.

0291. TATA INSTITUTE OF FUNDAMENTAL RESEARCH, **Basic Dental Research Unit, Homi Bhabha Road, Bombay 400 005, India.**

Project Title:
Intervention in the Tobacco Habits of Rural Indian Women.

Principal Investigators:
Aghi, M.B.; Mehta, F.S.

Objective:
To persuade rural Indian women to discontinue tobacco habits.

Methods or Approach:
A sample of approximately 12,000 individuals (each) from rural areas of Kerala and Andhra (3,581 and 6,514 women, respectively) are being persuaded to give up tobacco use through a concentrated program of motivation, education, and guidance for quitting. Strategies for women involve references to family and especially to children to appeal to mothers, emphasizing their responsibility to stay healthy to look after the family. Messages are communicated by talking to women individually. In addition, films, radio, posters, and newspaper articles are utilized to support, motivate, and educate. Intervention strategies are evaluated through impact studies and feedback is utilized to evolve new strategies. Individuals are examined annually to assess changes in tobacco habits, development of new oral precancerous lesions, and changes in precancerous diagnosed lesions.

Results to Date:
Results of fifth annual followup show that in Kerala and Andhra Pradesh, respectively, 16 and 17 percent of women stopped using tobacco, and 31 and 57 percent reduced tobacco consumption. There were marked changes in precancerous lesions in those who stopped or reduced tobacco use. In all followups, more women than men have given up the tobacco habit.

Project Dates:
July 1978–1985.

Financial Support:
USPHS (01-022-01).

0292. UNIVERSITY OF BOMBAY, SETH G.S. MEDICAL COLLEGE, **Department of Chest Medicine, K.E.M. Hospital, Parel, Bombay 420 012, India.**

Project Title:
Lung Function Norms in Indian Adults.

Principal Investigators:
Kamat, S.R.; Malhotra, M.S.; Tyagi, N.K., et al.

Objective:
To (1) establish normal lung functions in a large population of adult Indian subjects derived as a representative cross-sectional sample; (2) study the causes of reduced lung function in Indians compared to western subjects; (3) relate effects of smoking on lung function in Indian males; and (4) assess the role of respiratory infections in childhood, daily physical exertions, economic factors, and frequent colds on lung function in Indians.

Methods or Approach:
From the demographic census (1961) of Indian Nation and Tamil Nadu subjects, economic, occupational, and physical exertion data were collected and sample sizes determined. A sufficient number of nonsouthern Indians were included. Possibly abnormal subjects were excluded; normal subjects were studied clinically with several spirometric and gas exchange measurements. A comparison was made of normalcy predictions among Indians with other workers around the world. The relationship of lung function to smoking, daily

activity, history of chest and general illnesses, frequent colds, skin allergy, and economic status was assessed.

Results to Date:

Initial results showed that respiratory values in Indians were 20 to 24 percent lower than western white subjects, and age-related declines were slightly larger. For heavier-smoking subjects, lung functions were lower; moderate smokers had higher values. There was a significant relationship of forced expiratory volume in 1 sec to socioeconomic status. There was no relationship of function to daily physical activity, previous chest illnesses, frequent colds, or skin allergy. It is concluded that nutritional factors may account for lower lung function in India.

Future Plans:

A study of the relationship of lung function to smoking in patients with chronic bronchitis may be conducted.

Project Dates:

January 1966–August 1982.

Financial Support:

Defense Institute of Physiology and Allied Sciences; University of Bombay.

References:

(1) Kamat, S.R.; Sarma, B.S.; Raju, V.R.K., et al. "Indian Norms for Pulmonary Function: Observed Values, Prediction Equations, and Correlations." *Journal of the Association of Physicians of India* 25:531-540, 1977. (2) Kamat, R.R.; Tyagi, N.K.; Rashid, S.S.A. "Lung Function in Indian Adult Subjects." *Lung India* 1:11-21, 1982.

0293. UNIVERSITY OF BOMBAY, SETH G.S. MEDICAL COLLEGE, Department of Chest Medicine, K.E.M. Hospital, Bombay 420 012, India.

Project Title:

Prospective 3-Year Study of Health Morbidity and Cause–Effect Relationship With Air Pollution in Bombay, India.

Principal Investigators:

Kamat, S. R.; Shirodkar, V. B.

Objective:

To ascertain respiratory health abnormality in three urban areas (with high, medium, and low air pollution) and one rural area around Bombay by (1) monitoring SO_2, SPM and NO_2 levels in these areas; (2) following the health and lung function of the residents for 3 years; (3) assessing the effects of smoking, cooking fuel, housing, and nutrition on clinical abnormalities and lung function; (4) correlating the relationship of clinical and functional morbidity and yearly decline in lung function with air pollution; and (5) using discriminant analyses for establishing this relationship.

Methods or Approach:

A census was carried out in defined communities (without slums) and semimatched populations selected to reduce differences of age, sex, income, and duration of residence between four communities. A clinical respiratory questionnaire (MRC 1971) was administered and investigations with spirometry done. SO_2, SPM and NO_2 were monitored every fifth day in urban areas. Thus monthly followup and daily health diaries for respiratory symptoms were maintained. Meticulous assessment of housing, sanitation, diet, greenery, seasonal changes, and cooking fuel was undertaken. The data were analyzed by computer.

Results to Date:

Over 3 years, 53-60 percent of the urban and 44 percent of the rural subjects were followed. Significant respiratory morbidity such as frequent colds and intermittent cough was seen with high and medium SO_2 pollution. The frequency of cardiac diseases was higher in areas with high and low SO_2 pollution but with greater vehicle congestion. The rural communities showed intermediate morbidity. A protective effect of greenery was evident. Results show that expiratory flow rates, functional (FEV_1) declines were greater with pollution. Slum residents suffered higher morbidity. Daily health symptoms were related to SO_2 levels, with thresholds around 50 µg. Cancer and cardiorespiratory deaths were related to pollution. Food and water were heavily contaminated. Carboxyhemoglobin levels increased around heavier traffic and there was high morbidity in local residents. While nutrition, smoking, age, and fuel played a significant role in health, pollution was of great importance.

Future Plans:

An in-depth study of the effect of urbanization due to the new gas-based fertilizer project is planned to determine the degree of correlation between air pollution and health in developing cities of India.

Project Dates:

June 1976–April 1983.

Financial Support:

Bombay Municipal Corporation; MRC, India.

IRELAND

0294. ECONOMIC AND SOCIAL RESEARCH INSTITUTE, 4 Burlington Road, Dublin 4, Ireland.

Project Title:

Social-Psychological Factors Related to the Initiation and Maintenance of Drug, Alcohol, and Tobacco Use Among Post-Primary School Children.

Principal Investigators:

Grube, J.W.; Morgan, M.

Objective:

To (1) provide information about social-psychological processes that underlie experimentation with and use of tobacco, alcohol, and other drugs among postprimary schoolchildren in Dublin, Ireland; (2) examine interpersonal influences, including perceived attitudes and behaviors of parents and peers regarding smoking, drinking, and other substance use; (3) determine intrapersonal influences, including values, attitudes, beliefs, and personality; and (4) examine background influences, including family socioeconomic status, gender, and related characteristics; and (5) develop and test a multivariate and interactive model of substance use.

Methods or Approach:

The study consists of a three-wave panel design over a 1-year period. Data will be obtained using anonymous questionnaires administered to randomly selected classes in a sample (stratified for type of school, sex of students, and socioeconomic status) of 24 Dublin postprimary schools. Self-generated identification codes will be used to match data from the three testing sessions.

Results to Date:

In a pilot study of students aged 11 to 14 years, 66 percent of the boys and 35 percent of the girls reported that they had tried smoking. Current smoking rates were lower; 31 percent of boys and 13 percent of girls reported having smoked within the month prior to the survey. For both boys and girls, the most important predictors of future smoking intentions were perceived peer smoking and evaluation of the negative consequences of smoking. Parental smoking was also important for boys, and parental disapproval and perceived likelihood of negative consequences of smoking were important for girls.

Project Dates:
February 1984–November 1985.

Financial Support:
Commission of the European Communities, Directorate-General Employment, Social Affairs and Education; Economic and Social Research Institute, Dublin.

Reference:
Grube, J.W.; McGree, S.; Morgan, M. "Smoking Behaviours, Intentions and Beliefs Among Dublin Primary School Children." *Economic and Social Review* 15:265-288, 1984.

0295. SOCIAL RESEARCH CENTER, N.I.H.E., Plassey Technological Park, Limerick, Ireland.

Project Title:
National Study of Smoking and Drinking Behaviour. Social and Cultural Influences.

Principal Investigators:
O'Connor, J.; Daly, M.

Objective:
To (1) provide a nationwide picture of smoking habits and attitudes; (2) provide a nationwide picture of drinking behavior; (3) increase understanding of the social factors that influence smoking behavior and attitudes; and (4) indicate key target groups for specific health education programs.

Methods or Approach:
A representative sample of 2,724 persons aged 18 and over were interviewed. Nonresponse rate was between 3 percent and 8 percent. The study is the first stage of a long-term research program to help further the aims of the Health Education Bureau's policy formation in the areas of smoking and drinking behavior. Preliminary research consisted of a series of informal, in-depth interviews and discussions with a sample of individuals, followed by a series of pilot studies, to select items for the formulation of attitude scales and to provide measures of relevant variables. After pretesting, changes were made to the questionnaire. Fieldwork for the major study was completed between October and December 1980.

Results to Date:
Findings raise the following issues in need of debate and action: (1) patterns of cigarette smoking vary considerably, principally between males and females, different age groups, occupational groupings, and urban and rural areas, indicating the need to differentiate between target groups for smoking control purposes; (2) smokers smoke for different reasons, suggesting the need to differentiate between different types of smokers in any health education campaign; (3) the many people who experiment with smoking form an ideal target group for primary prevention and secondary intervention; (4) smoking is a minority behavior pattern; however, most people believe that nonsmokers are the minority group; (5) cigarette consumption is a public health issue since nearly all cigarette smokers smoke on a regular basis and half are classified as heavy smokers; (6) the social climate surrounding smoking in Ireland is favorable and there is a high level of social support for smoking; (7) there is widespread exposure to passive smoking and the resulting effects on health need to be addressed; (8) the question of substance abuse, in particular the relationship between smoking and drinking behavior, needs to be integrated into health education programs; and (9) the prevalence of alcohol-related problems is also a cause for concern.

Financial Support:
Health Education Bureau, Ireland.

0296. ST. LUKE'S HOSPITAL, UNIVERSITY COLLEGE, Department of Community Medicine and Epidemiology, Earlsfort Terrace, Dublin 2, Ireland.

Project Title:
Role of Tobacco and Alcohol in the Etiology of Lung and Larynx Cancer.

Principal Investigators:
Herity, B.; Moriarity, M.; Bourke, G.J., et al.

Objective:
To examine the differential effects of exposure to cigarettes and alcohol in the etiology of laryngeal and lung cancer.

Methods or Approach:
This is a retrospective case–control study of 59 cases of lung cancer, 59 cases of laryngeal cancer, and 152 controls. All patients are males.

Results to Date:
Lung cancer patients smoked significantly more but drank significantly less than laryngeal cancer patients, while both groups smoked and drank more heavily than controls. A synergistic effect between alcohol and tobacco consumption was apparent in laryngeal cancer etiology, although drinking was shown to have no effect on lung cancer incidence when smoking was controlled for. The project is completed and results have been submitted for publication.

Project Dates:
1976–1982.

Financial Support:
St. Luke's Hospital.

0297. ST. VINCENT'S HOSPITAL, Cardiac Department, Elm Park, Dublin 4, Ireland.

Project Title:
Prevalence of Coronary Risk Factors, Including Tobacco Smoking, in Different Educational Groups in Ireland.

Principal Investigators:
Mulcahy, R.; Hickey, N.; Graham, I., et al.

Objective:
To determine the prevalence of coronary risk factors (smoking, hypertension, hypercholesteremia, obesity, and abnormal ECG) in higher educational groups.

Methods or Approach:
The Irish Heart Foundation risk factor screening service (MEDISCAN) is being used to provide data and assess the risk factor status of 5,000 males and 2,000 females of the community and industrial populations.

Results to Date:
Preliminary results confirm that subjects with a third-level education smoke less, have lower blood pressure and cholesterol levels, and are lighter and taller than first-level education subjects. Subjects with second-level education occupy medial positions.

Future Plans:
The study will be continued.

Project Dates:
1975–1985.

Financial Support:
Irish Heart Foundation; private donations; industry.

0298. ST. VINCENT'S HOSPITAL, Department of Preventive Cardiology and Cardiac Department, Elm Park, Dublin 4, Ireland.

Project Title:
Relationship of Smoking to Other Risk Factors and to In-Hospital Outcome in Acute Coronary Disease.

Principal Investigators:
Mulcahy, R.; Hickey, N.; Daly, L., et al.
Objective:
To characterize etiology, acute manifestations, and short-term prognosis of coronary heart disease in smokers.
Methods or Approach:
Patients admitted with myocardial infarction or unstable angina, confirmed by serial ECG changes, are being studied. Between January 1980 and December 1984, 898 male and 415 female patients of all ages were recruited. Multivariate techniques will be used to characterize risk factor profiles of smokers, ex-smokers, and nonsmokers and to assess relationship of smoking to prognosis.
Results to Date:
Preliminary data indicate greater frequency of anterior infarctions among nonsmokers. Current smokers are significantly younger than ex-smokers or nonsmokers. Among patients with unstable angina, smoking was associated with less persistent rest pain and a lower proportion of smokers had chronic angina of effort prior to hospital admission. Preliminary analysis suggests a marginally lower in-hospital mortality rate among smokers after controlling for age and other prognostic factors.
Future Plans:
Sex and preinfarction angina will also be examined as predictors of prognosis.
Project Dates:
January 1980–December 1986.

0299. ST. VINCENT'S HOSPITAL, Department of Preventive Cardiology and Cardiac Department, Elm Park, Dublin 4, Ireland.

Project Title:
Factors Predicting Successful Smoking Cessation in Survivors of a First Episode of Acute Coronary Heart Disease.

Principal Investigators:
Mulcahy, R.; Hickey, N.; Daly, L., et al.
Objective:
To identify patient subgroups in which smoking cessation rates are low; identify possible causal variables.
Methods or Approach:
Although smoking cessation following an episode of acute coronary heart disease offers a substantial improvement in 15-year prognosis, at least 30 percent of smokers fail to quit. A total of 1,082 male and 119 female patients (under 60 years of age) who survived a first myocardial infarction or bout of unstable angina are included in the long-term followup study. Patients are seen at least annually and smoking habits are recorded. Thiocyanate measurements are made in subsamples to assess veracity.
Results to Date:
Smoking cessation rates are higher among younger patients, better educated patients, and white-collar workers. Differences become more marked with increasing time since discharge. Preliminary analysis of psychological profiles indicates that patients with a high level of neurotic symptoms during hospital admission have a lower cessation rate.
Future Plans:
Studies of staff-patient communication and health beliefs of patients are planned.
Project Dates:
1961–continuing.

0300. ST. VINCENT'S HOSPITAL, Department of Preventive Cardiology and Cardiac Department, Elm Park, Dublin 4, Ireland.

Project Title:
Influence of Cigarette Smoking on Prognosis in Patients With Coronary Heart Disease.

Principal Investigators:
Mulcahy, R.; Hickey, N.; Daly, L., et al.
Objective:
To determine effect of cessation or reduction of cigarette smoking in patients following first myocardial infarction; compare long-term morbidity (angina of effort, unstable angina, and nonfatal myocardial infarction), mortality (coronary and all causes), and mode of death of patients who stop smoking following a coronary attack with those who continue to smoke.
Methods or Approach:
The cohort consists of 1,082 male and 119 female patients (under 60 years of age) who have recovered from a first bout of unstable angina or myocardial infarction and are participating in a long-term followup study. All were seen between 1961 and 1984, and each is seen annually and given a careful risk factor assessment. Influence of changes in cigarette smoking and of other risk factor interventions on long-term prognosis is assessed. Mode of death is recorded. The first patients have been followed for 24 years.
Results to Date:
The 15-year mortality of patients who stopped smoking following a coronary attack is 36.9 percent, less than half that of patients who continued to smoke (82.1 percent). The 15-year mortality of initial nonsmokers was 62.1 percent. Mode of death in survivors is not influenced by smoking status at time of followup. Postinfarction angina is less common in those who stop smoking than in those who continue to smoke, at least during the first 6 years of followup. The differences does not appear to be significant after 6 years.
Project Dates:
1961–continuing.

0301. ST. VINCENT'S HOSPITAL, Department of Preventive Cardiology and Cardiac Department, Elm Park, Dublin 4, Ireland.

Project Title:
Influence of Pipe and Cigar Smoking on Prognosis in Patients With Coronary Heart Disease.

Principal Investigators:
Mulcahy, R.; Hickey, N.; Daly, L., et al.
Objective:
To determine effects of cigar and pipe smoking on prognosis in survivors of unstable angina and myocardial infarction.
Methods or Approach:
Patients (1,082 males and 119 females, under 60 years of age) who survived a first bout of unstable angina or myocardial infarction are included in the long-term followup study. All patients were seen between 1961 and 1984. Each patient is seen at least annually and given a careful risk factor assessment. The influence of pipe and cigar smoking on morbidity,

mortality, and mode of death during followup is being examined.

Results to Date:
A preliminary study confirms that cigar smoking after myocardial infarction is associated with the same long-term mortality as continuing cigarette smoking. However, pipe smokers appear to have the same long-term mortality as initial cigarette smokers who quit smoking.

Project Dates:
1961–continuing.

0302. TRINITY COLLEGE, DUBLIN, Department of Clinical Medicine, TCD Medical School Building, St. James' Hospital, Dublin 8, Ireland.

Project Title:
Elastolytic Activity of Alveolar Macrophages in Chronic Bronchitis: Comparison of Current and Former Smokers.

Principal Investigators:
O'Neill, S.; Prichard, J.S.

Objective:
To compare macrophage elastolytic activity of a group of current and ex-smokers with irreversible air flow obstruction; investigate whether enhanced macrophage elastolytic activity alone is a determining factor in susceptibility of some smokers to obstructive lung disease.

Methods or Approach:
Elastolytic activity was determined in an initial bronchoalveolar lavage cell population and in alveolar macrophages cultured for 3 days. Subjects were 20 smokers and 12 ex-smokers who had been abstinent for at least 3 years. All patients had spirometric evidence of irreversible air flow obstruction.

Results to Date:
After 3 days in culture, macrophage elastolytic activity was considerably greater in cells from smokers than in cells from ex-smokers. Elastase activity of cultured alveolar macrophages from five current smokers had the inhibitor profile of a metallo-proteinase.

Project Dates:
February 1981–January 1983.

Financial Support:
Wellcome Foundation, London.

Reference:
O'Neill, S.; Prichard, J.S. "Elastolytic Activity of Alveolar Macrophages in Chronic Bronchitis: Comparison of Current and Former Smokers." *Thorax* 38:356-359, 1983.

0303. UNIVERSITY COLLEGE DUBLIN, Department of Community Medicine and Epidemiology, Earlsfort Terrace, Dublin (01) 755114, Ireland.

Project Title:
Ten-Year Followup of Industrial Screenees.

Principal Investigators:
Daly, L.; Graham, I.; Hickey, N., et al.

Objective:
To relate baseline cardiovascular risk factors, including smoking, to 10-year mortality in a group of individuals who underwent an industry-based screening program.

Methods or Approach:
Male industrial workers (n = 2,777), who underwent a comprehensive risk factor screening in 1970 to 1972, have been followed up for 10 years. Mortality will be related to factors measured at the initial examination using logistic regression and Cox's lifetable analysis.

Results to Date:
Results are not yet available.

Project Dates:
January 1970–December 1985.

Financial Support:
Irish Heart Foundation.

ISRAEL

0304. BEN-GURION UNIVERSITY OF THE NEGEV, Epidemiology and Health Services Evaluation Unit, P.O. Box 653, Beer Sheva 84 105, Israel.

Project Title:
Prevention of Smoking and Its Health Effects in the Negev Region of Israel.

Principal Investigators:
Goldsmith, J.R.; Levy, E.; Ben-Tal, T.

Objective:
To (1) strengthen the effect of smoking monitoring and advice in the Mother and Child clinics; (2) provide materials and work with public schools; (3) work with peer groups; (4) offer smoking cessation courses; and (5) work with community organizations.

Methods or Approach:
The staff meets with nurses and physicians, counsels patients, and puts pressure on the health department to use its influence in clinic operations. A survey was conducted in 1982 of all high school students to determine smoking practices, sources of information, and motivation to change smoking behavior. A volunteer group of medical students meets with primary and secondary school students to inform them of the health risks of smoking, and the staff works with teachers. A new law forbids smoking in public places, but there are no penalties. Hospital and clinic smoking constraints are being worked out. In the university, a code of conduct is being developed, targeting physicians, nurses, teachers, and police as peer groups. Smoking cessation courses are being offered and information is being provided to neighborhood groups, individuals, and the press.

Results to Date:
Smoking cessation courses have had the expected 30 percent long-term success rate. Technical support for use of the Carboximeter became a problem, but it did provide data suggesting that as smokers reduce the number of cigarettes, the average dose of carbon monoxide does not drop as rapidly. From the high school survey, it was learned that many smokers are already seeking help to stop smoking.

Future Plans:
Two supplementary projects will be to (1) systematically evaluate the program, based on periodic surveys of the smoking practices of the general public, medical center staff, women at time of delivery, and high school students; and (2) prepare, utilize, and evaluate new health education materials that emphasize more immediate effects of smoking rather than those on cancer and heart disease, particularly effects on

reproductive outcome and respiratory disease of infancy associated with parental smoking.

Project Dates:
October 1982–continuing.

Financial Support:
Ben-Gurion University of the Negev; Israeli Cancer Society.

0305. CARMEL HOSPITAL, FACULTY OF MEDICINE, Department of Family and Community Health, 7 Michal Street, Haifa 34362, Israel.

Project Title:
Health Related Behavior of Israel Adolescents.

Principal Investigators:
Epstein, L.; Tamir, A.

Objective:
To (1) determine the extent and correlates of health-related behavior in Israeli adolescents (smoking, drugs, sexual activity, use of medicines, alcohol, and diet); (2) determine the interrelationship between behavioral attributes; and (3) determine changes in behavior over time, and the correlates.

Methods or Approach:
Physical examination and interviews of 804 secondary school students were conducted in 1978-1979, and reinterviews of one-third of the students were completed 2 years later.

Results to Date:
Study data indicated (1) a cross-sectional and longitudinal health relationship between smoking and other behavioral attributes; (2) a relationship between smoking and parental and friends' smoking and respiratory symptoms; (3) a negative relationship between smoking and blood pressure in nonobese adolescents; (4) a relationship between smoking and dropping out of school; and (5) a relationship between age of starting to smoke and development of sexual activity.

Future Plans:
A major project is planned in which a cohort of adolescents will be followed from age 10 to determine the processes of behavioral development. Intervention is also being considered.

Project Dates:
1978–continuing.

0306. CARMEL HOSPITAL, FACULTY OF MEDICINE, Department of Family and Community Health, 7 Michal Street, Haifa 34362, Israel.

Project Title:
Health Related Behavior of Arab-Israeli Adolescents.

Principal Investigators:
Tamir, A.; Epstein, L.

Objective:
To (1) determine extent and correlates of health-related behavior in Arab-Israeli adolescents (smoking, drugs, use of medicines, alcohol, and diet); (2) determine interrelationship between behavioral attributes; and (3) compare health-related behaviors of Arab and Jewish Israeli adolescents.

Methods or Approach:
Physical examinations and interviews were conducted in 1984 of 658 students in an Arabic regional high school.

Results to Date:
Results are not yet available.

Project Dates:
April 1984–October 1985.

Financial Support:
Carmel Hospital, Israel.

0307. CARMEL HOSPITAL, FACULTY OF MEDICINE, Department of Family and Community Health, 7 Michal Street, Haifa 34362, Israel.

Project Title:
Case–Control Study of the Possible Causes of the Differences in Lung Cancer Incidence Rates in Towns in Israel.

Principal Investigators:
Tamir, A.; Epstein, L.

Objective:
To determine if differences in incidence rates for lung cancer between towns in Israel can be explained by differences in (1) smoking habits, (2) occupational exposure, or (3) exposure to air pollutants.

Methods or Approach:
For a 2-year period, all patients with diagnosed lung cancer and matched controls in three towns in Israel will be interviewed. Data will be collected relating to smoking habits, passive exposure to smoke, occupational history, and all places subjects have lived.

Results to Date:
In a previous study for the period from 1960 to 1974, differences were found in incidence rates of lung cancer. Initial findings of the present study confirm that differences still exist.

Project Dates:
January 1984–June 1986.

Financial Support:
Carmel Hospital, Israel; Israel Cancer Society; Sapir Foundation.

0308. CHAIM SHEBA MEDICAL CENTER, Section of Epidemiology Heart Institute, Tel-Hashomer 52621, Israel.

Project Title:
15-Year Mortality Follow-Up of the Israeli IHD Cohort.

Principal Investigator:
Goldbourt, U.

Objective:
To (1) evaluate the quantitative role of several risk factors in predicting 15-year mortality (1963-1978); (2) identify ethnic pattern and seek explanations; and (3) relate coronary risk factors to deaths from coronary heart disease (CHD), cancer, stroke, and all causes.

Methods or Approach:
Mortality was ascertained by matching ID numbers with the national mortality registry. Mortality rates were calculated in quintiles of numerical variables and in categories of categorical variables (including smoking). Estimated relative risks and associated confidence intervals were calculated by the Cox proportional hazards model.

Results to Date:
Among the 10,059 men aged 40 or over who constitute the cohort study (tenured civil servants and municipal employees), 1,664 deaths were identified over the 15 years, including 618 deaths from CHD and 369 from cancer. Cigarette smoking was a significant predictor of both total and cancer mortality. Estimated relative risk of dying over the 15 years, among those who smoked 11 to 20 cigarettes/day, was 1.67 (95 percent confidence interval, 1.51 to 1.85). Estimated relative risk of dying from cancer, related to smoking 11 to 20 cigarettes/day compared with risk among nonsmokers, was 1.84 (95 percent confidence interval, 1.49 to 2.28).

Future Plans:
The role of smoking in predicting stroke mortality will be analyzed, and comparative risks associated with smoking in

different age and ethnic groups will be examined. Risk associated with smoking in hypertensive patients, diabetics, and in men after myocardial infarction will also be studied as will interactions between smoking, relative weight, and lipoproteins.
Project Dates:
1980–December 1986.
Financial Support:
National Academy of Sciences, Jerusalem; Tel-Aviv University, Sackler School of Medicine.

0309. GOLDA MEDICAL CENTER, Petach-Tiqva, Israel.

Project Title:
The Project for the Study and Control of Atherosclerosis Precursors in Children, Young Adults and Their Families.

Principal Investigator:
Zahavi, I.
Objective:
To survey all cardiovascular risk factors in children and their parents in different ethnic groups; promote changes in life habits among children and their parents, including control of smoking.
Methods or Approach:
Children in the 4th and 11th grades are interviewed by a questionnaire covering general health and lifestyle habits (diet, smoking) and behavior type. The same questionnaire is distributed to parents of the children. Parents and children are examined and blood is drawn for several tests, including glucose and lipids.
Results to Date:
Project is in a preliminary phase.
Project Dates:
October 1984–October 1987.

0310. HAIFA UNIVERSITY, ORANIM SCHOOL OF EDUCATION OF THE KIBBUTZ MOVEMENT, Department of Science Education, Division of Chemical Studies, Kiryat Tivon 36910, Israel.

Project Title:
Effectiveness Evaluation of the Modified "Smoking and Cigarette Smoke" Curriculum (MSACS): Smoking Behavior, Attitudes and Values.

Principal Investigators:
Maymon, T.; Zoller, U.
Objective:
To evaluate effectiveness of the MSACS curriculum in achieving its main objective: prevention of smoking among Israeli secondary school students.
Methods or Approach:
Subjects were students aged 15 and 16 years from five urban secondary schools, who had different backgrounds. A pretest/posttest design was used. Two intact classes from each school were randomly assigned to either experimental ($n = 170$) or control ($n = 170$) groups. All students were administered the same evaluation instrument in the pretest and posttest (2 months apart). The instrument tested smoking behavior and related predisposition factors (attitudes, values, and perceptions). Statistical tests applied were chi-square analysis and the t-test for independent sampling.
Results to Date:
Chi-square analysis showed significant difference in smoking behavior of students exposed to MSACS compared with controls. A significant difference was found in the number of new smokers in the control group compared with the number of new smokers in the experimental group. T-tests showed significant differences in the desired direction in most of the categories that constitute the attitude scale, but not in all. Changes of values and perceptions were not found. Modification of attitudes, values, and perceptions in the desired direction served as indicators of the effectiveness of the program concerning future smoking behavior of participants.
Future Plans:
Improvements will be made in the MSACS and in the evaluation instrument. The program will be implemented throughout the country's school system.
Project Dates:
January 1982–October 1983.
Financial Support:
Israel Cancer Association.

0311. HAIFA UNIVERSITY, ORANIM SCHOOL OF EDUCATION OF THE KIBBUTZ MOVEMENT, Department of Science Education, Division of Chemical Studies, P.O. Kiryat Tivon 36910, Israel.

Project Title:
Implementation, Activation and Evaluation of the Preventive Program "Smoking and Cigarette Smoke."

Principal Investigator:
Zoller, U.
Objective:
To assess the smoking attitudes and behavior of high school students in Israel; evaluate impact and effectiveness of the interdisciplinary science and decisionmaking oriented curricular unit "Smoking and Cigarette Smoke" on the smoking attitudes, values, and behavior of high school students.
Methods or Approach:
The special curriculum has been developed and implemented in high schools, within ongoing science courses (mainly biology and chemistry). About 3,300 students and 40 teachers in 25 representative high schools around the country participated in the study. Participants (including control classes) completed pre- and postreatment questionnaires on smoking attitudes and behavior.
Results to Date:
It was found that smoking behavior (and age distribution) of high school students in Israel is comparable with that of high school students in the United States; however, reasons for smoking and not smoking as perceived by the students are different in the two countries both qualitatively and quantitatively. It was also found that the curriculum unit significantly and effectively affects smoking attitudes and values of participating high school students. The treatment also inhibits the "natural" increase of smoking among high school students.
Project Dates:
1979–1982.
Financial Support:
Israel Cancer Association (13/81/A).
References:
(1) Zoller, U. "Smoking and Cigarette Smoke. An Innovative, Interdisciplinary, Chemically-Oriented Curriculum." *Journal of Chemical Education* 56(8):518-519, 1979. (2) Zoller, U.; Maymon, T. "Smoking Behavior of High School Students in Israel." *Journal of School Health* 53(10):613-617, December 1983.

0312. HEBREW UNIVERSITY, SCHOOL OF PUBLIC HEALTH AND COMMUNITY MEDICINE, Department of Social Medicine, P.O. Box 1172, Jerusalem 91010, Israel.

Project Title:
Identification of a Community Program for Reduction of Smoking and Other Cardiovascular Risk Factors.

Principal Investigators:
Abramson, J.H.; Laaser, U.; Peritz, E., et al.
Objective:
To (1) evaluate a long-term community health program conducted within the framework of primary care; (2) analyze correlates of smoking habits and changes in smoking habits; and (3) study relationships between smoking and other characteristics.
Methods or Approach:
Smoking habits and other cardiovascular risk factors in 1985-1986 will be compared with data for the same community gathered in 1974 and 1976.
Results to Date:
Data from the current study are not yet available, but earlier evaluations have demonstrated considerable reduction in cigarette smoking.
Project Dates:
1984–1987.
Financial Support:
National Council for Research and Development, Israel; G.S.F. Munchen, Federal Republic of Germany.

0313. KIBBUTZ GIVAL HAIM ICHUD, Gival Haim Ichud, Israel.

Project Title:
Physician Intervention in Smoking Cessation in a Kibbutz Community.

Principal Investigator:
Dlin, R.
Objective:
To determine effects of intervention by an attending physician on smoking habits of members of a close-knit cooperative agricultural community.
Methods or Approach:
The kibbutz is a close-knit agricultural community that operates as a cooperative, with individuals living and working within the community. There is only one attending physician, who lives within the community. An effort was made to improve community awareness of the detrimental effects of smoking by (1) discussion of health hazards in the primary health care office setting; (2) publication of articles in the community newpaper; and (3) use of posters as reminders of the effects of smoking.
Results to Date:
Followup in the 5 years since initiation of the program shows a 32.4 percent reduction in the number of smokers in the Kibbutz. During the same period, no significant changes were noted in smoking habits of the general population of Israel.
Future Plans:
Programs will be initiated to prevent young people from starting to smoke. Followup of the cessation-oriented program will continue.

0314. TEL AVIV UNIVERSITY, SACKLER FACULTY OF MEDICINE, School of Dental Medicine, 69978 Ramat Aviv, Tel Aviv, Israel.

Project Title:
The Effect of Tobacco Smoking in Melanin Pigmentation in the Oral Mucosa of the Israeli Jews.

Principal Investigators:
Gorsky, M.; Buchner, A.; Begleiter, A.
Objective:
To study the special influence of tobacco smoking on oral pigmentation.
Methods or Approach:
In a previous study, oral pigmentation was observed in 35.6 percent of a sample of Israeli Jews. The prevalence of oral pigmentation will be compared between two main groups of Israeli Jews: smokers and nonsmokers. The influence of smoking on pigmentation will be analyzed statistically to determine significance.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–December 1985.
Financial Support:
Tel Aviv University.

0315. TEL AVIV UNIVERSITY, SACKLER FACULTY OF MEDICINE, Department of Preventive and Social Medicine, 69978 Ramat Aviv, Tel Aviv, Israel.

Project Title:
Comparison of Sexual Dysfunction Complaints in Smokers vs. Nonsmokers.

Principal Investigators:
Carel, R.; Papier, C.
Objective:
To evaluate whether complaints of sexual dysfunction are more frequent among smokers than nonsmokers; investigate whether there is a quantitative relationship between level of smoking and degree of complaint.
Methods or Approach:
In the planned case–control study, groups of current smokers and nonsmokers will be compared with respect to level of complaint of sexual dysfunction. Groups will be selected from a large computerized data base of many employed groups of workers in Israel. All the people underwent comprehensive health appraisal between 1976 and 1984, including a computerized medical history questionnaire. Among other items, the questionnaire contained items related to smoking habits and sexual disturbances. From each examinee's record, pertinent demographic, physiological, psychological, and other variables will be extracted. Groups will be matched and compared for various confounding variables and then compared according to level of smoking and sexual dysfunction.
Results to Date:
Project is in a preliminary phase.
Future Plans:
If findings support the research hypothesis, they will be used to develop educational programs to deal with the problem.
Project Dates:
October 1984–October 1985.
Financial Support:
Tel Aviv University.

0316. WINGATE INSTITUTE, Department of Research and Sports Medicine, Wingate Post, Israel.

Project Title:
Smoking Habits of Competitive Sportsmen.

Principal Investigators:
Dlin, R.; Tannenbaum, G.; Hanne, N.
Objective:
To evaluate frequency distribution of smoking among competitive athletes.
Methods or Approach:
Medical records of 2,800 competitive sportsmen at all levels of competition in various sports were examined for smoking history, age, and fitness characteristics.
Results to Date:
Soccer players had the highest percentage of smokers when groups were compared according to training. Ball sport groups showed the highest percentage of smokers, followed by skill sports and strength sports. The lowest percentage of smokers was found in athletes trained for endurance. Higher achievement athletes smoked significantly less than lower achievers. Nonsmokers had significantly higher VO_2 max than smokers or ex-smokers.
Future Plans:
Intervention programs are planned to prevent young athletes from starting to smoke.
Project Dates:
May 1984–March 1985.
Financial Support:
Wingate Institute, Israel.

ITALY

0317. CATTEDRA DI EPIDEMIOLOGIA DEI TUMORI, Via Santena 7, 10126 Torino, Italy.

Project Title:
Case–Control Study on Childhood Leukemia and Soft-Tissue Sarcoma.

Principal Investigators:
Magnani, C.; Pastore, G.; Luzzatto, L., et al.
Objective:
To (1) investigate role of smoking habits and occupation; (2) examine x-ray exposure of children and parents; and (3) investigate epilepsy and antiepileptic treatment.
Methods or Approach:
The project is a hospital-based case–control study of soft-tissue sarcoma and leukemia in children (under 14 years of age at time of diagnosis). The 182 cases of leukemia are hospitalized in the main pediatric oncology unit in Piedmont; 25 cases of soft-tissue sarcoma are hospitalized in the same unit and 28 cases in a similar unit in Padova, Veneto. Two control groups have been identified from children admitted to the same hospitals for non-neoplastic diseases (307 in Torino and 58 in Padova). Parents of cases and controls are interviewed.
Results to Date:
Interviews have been completed; analyses will be carried out in 1985.
Project Dates:
January 1982–June 1985.
Financial Support:
Consiglio Nazionale Delle Ricerche, Progetto Finalizzato Oncologia - 83 (83.00960.96); Regione Piemonte; Associazione Italiana per la Ricerca sul Cancro.

0318. GENERAL HOSPITAL OF MONFALCONE, Laboratory of Pathological Anatomy, Via Rossini 1, 34074 Monfalcone, Italy.

Project Title:
Malignant Mesothelioma of the Pleura in the Monfalcone Area.

Principal Investigators:
Bianchi, C.; Brollo, A.; Bittesini, L.
Objective:
To collect and analyze all cases of malignant pleural mesothelioma observed at the Monfalcone Hospital.
Methods or Approach:
Occupational history and data on smoking habits are obtained from the patients or relatives by personal interview. Special attention is devoted to asbestos exposure from occupation or other sources.
Results to Date:
Results are not yet available.
Project Dates:
October 1979–continuing.
Financial Support:
General Hospital of Monfalcone.

0319. INSTITUTO NAZIONALE DEI TUMORI, ONCOLOGY CLINIC, Via G. Venezian 1, 20133 Milano, Italy.

Project Title:
The Growth Rate in the Interpretation of the Natural History of Lung Cancer.

Principal Investigators:
Galante, E.; Reduzzi, D.; Gallus, G., et al.
Objective:
To (1) evaluate the natural history of lung cancer by use of the growth characteristic as a fundamental parameter; (2) assess if and how biological (age and sex) or environmental factors (smoking) influence growth rate; and (3) determine whether there is a relationship between growth rate and clinical appearance (mode of detection), dimensional stage (size), and ability to metastasize (lymph node involvement).
Methods or Approach:
Subjects were 110 patients with lung cancer admitted to the Instituto Nazionale Tumori of Milan from 1979 to 1983. Two or more serial radiological examinations of the chest, performed with an interval of more than 30 days, were available for all patients. Cell types were 34 epidermoid carcinomas, 57 adenocarcinomas, 6 large cell carcinomas, 3 small cell carcinomas, 1 malignant carcinoma, 1 carcinoma, 1 adenosquamous carcinoma, and 7 malignant tumors only cytologically defined. The relationship between growth rate, expressed as doubling time (DT) and age, sex, histological type, symptoms, smoking habits, size, and lymph node involvement was investigated.
Results to Date:
Median DT values of epidermoid carcinomas and adenocarcinomas were superimposable (98 and 99 days, respectively), but

15 percent of adenocarcinomas had a DT of more than 1 year. Significant correlations were found for sex (slower growth rate in females) and symptoms (faster growth in symptomatic patients), but only for adenocarcinomas. Smoking as a promoter of lung cancer is not questioned, but it does not seem to enhance tumor growth rate. There was no correlation between growth rate and tumor size of lymph node involvement.

Reference:

Galante, E.; Reduzzi, D.; Gallus, G., et al. "The Growth Rate in the Interpretation of the Natural History of Lung Cancer." *Tumori* 70:427-432, 1984.

0320. INSTITUTO NAZIONALE DEI TUMORI, Via Venezian 1, 20133 Milan, Italy.

Project Title:

Different Patterns of Lung Cancer Risk in Relation to Evolving Smoking Habits in Italy.

Principal Investigators:

Berrino, F.; Pisani, P.; Crosignani, P.

Objective:

To establish relative risks of different types of cigarettes (blond/black tobacco, filtered/nonfiltered) in etiology of lung cancer; estimate reduction in risk in relation to quitting smoking, switching to low-tar cigarettes, and lowering amount smoked.

Methods or Approach:

As part of an international collaborative study, detailed interviews on lifelong smoking habits have been conducted with 1,247 incident cases and 2,650 hospital controls (free of other tobacco-related diseases). Questions on smoking include amount, duration, and brand for up to four different smoking periods; information on age of initiation, time since quitting, and use of cigars and pipes is also recorded.

Results to Date:

Results are not yet available.

Project Dates:

January 1978–December 1985.

Financial Support:

NCI (NO1-CP-05644); Consiglio Nazionale delle Ricerche, Progetto Finalizzato Oncologia (84.00448.44).

0321. ISTITUTO DI RICERCHE FARMACOLOGICHE "MARIO NEGRI," Via Eritrea 62, 20157 Milan, Italy.

Project Title:

Vascular Effect of Smoke and/or Oral Contraceptive Treatment.

Principal Investigators:

Donati, M.B.; Poggi, A.; Dejana, E.

Objective:

To investigate whether oral contraceptives (OC) or cigarette smoke (or both) influence cells of the vascular wall in the ability to release prostacyclin and to proliferate; (2) investigate whether treatment with OC, alone or in combination with smoke, would modify mitogenic activity of serum, considered a biological measure of platelet derived growth factor (PDGF); and (3) compare effect with serum ability to stimulate prostacyclin production.

Methods or Approach:

Whole blood serum was obtained from healthy women (20 to 30 years old) divided into four groups: normals, smokers, OC users, and smokers who used OCs. Serum (50 percent V/V) was added to quiescent rat aortic smooth muscle cells and incubated for 18 hours. Stimulation of DNA synthesis was evaluated as ^{3}H-thymidine incorporation, measured by TCA precipitable radioactivity. Production of prostacyclin was determined by radioimmunoassay as amount of stable metabolite 6-keto-PDGF$_{1\alpha}$ released into medium. Cell proliferation was measured as increase of cell number at daily intervals.

Results to Date:

Cigarette smoking significantly reduced serum ability to stimulate ^{3}H-thymidine incorporation and proliferation of smooth muscle cells was significantly reduced in smokers compared with controls. The inhibitory effect was almost completely abolished by simultaneous use of OC. Serum from smokers enhanced prostacyclin production from cells, independently of OC use. It is possible that smoking might induce release of a toxic factor in serum that is able to antagonize the effects of PDGF.

Future Plans:

Investigations will include the origin of the toxic factor for smooth muscle cells found in serum of women who smoke, and whether a similar factor is present in serum of men or women in association with other risk factors such as age and obesity.

Project Dates:

August 1983–July 1988.

Financial Support:

Italian National Research Council (8302620.56).

0322. ISTITUTO DI RICERCHE FARMACOLOGICHE "MARIO NEGRI," Via Eritrea 62, 20157 Milan, Italy.

Project Title:

Effects of Maternal Smoking on Success Rate of Cultured Endothelial Cells and Their Production of Fibronectin and Release of PGI$_2$ in Culture Medium.

Principal Investigators:

Dejana, E.; Colella, S.; Breviario, F., et al.

Objective:

To study effects of maternal smoking on fetal endothelial cell activities; (2) examine success rate of cultured endothelial cells obtained from umbilical veins of infants born to mothers who smoke; (3) quantitate prostacyclin production; and (4) study fibronectin synthesis and organization by cultured endothelial cells.

Methods or Approach:

Methods included (1) in vitro culture of endothelial cells; (2) measurement of adhesion efficiency and growth parameters on cells obtained from umbilical cords of infants born to heavy smokers ($>$15 cigarettes/day), mild smokers ($<$15 cigarettes/day), and nonsmokers; (3) prostacyclin production by cells, measured in cultured medium by radioimmunoassay; (4) fibronectin released in culture medium, measured by specific solid phase radioimmunoassay; and (5) fibronectin organization and distribution, measured by immunofluorescent technique.

Results to Date:

Endothelial cells obtained from umbilical veins of infants born to mild and heavy smokers were significantly less able to grow and to reach confluency than cells from nonsmokers. Smoking was also a factor in the reduced capacity of cultured cells to produce PGI$_2$, particularly apparent for cells from heavy smokers. Smoking during pregnancy appears to induce modifications in enzymes of the prostacyclin pathway that persist in endothelial cells undergoing replication in primary culture, even in the absence of the pathogenic factor.

Future Plans:

The amount of fibronectin production and its organization in endothelial cells will be evaluated; a possible relationship with the decreased ability of endothelial cells from mothers who smoke to adhere and grow in culture will be investigated.

Project Dates:
January 1982–January 1987.

Financial Support:
Regione Lombardia, Italy.

0323. ISTITUTO MALATTIE RESPIRATORIE DELL' UNIVERSITA, Policlinico, Via Francesco Sforza 35, 20122 Milano, Italy.

Project Title:
Smoking Habit and Rheological Properties of Bronchial Fluids.

Principal Investigators:
Allegra, L.; Braga, P.; Bossi, R., et al.

Objective:
To (1) select and examine patients with chronic bronchitis; (2) correlate smoking habits with rheology of sputum; and (3) assess possible pharmacological prevention or correction of rheological dysfunctions or mucociliary disturbance due to smoking.

Methods or Approach:
Questionnaires are used to select patients with chronic bronchitis and smoking habits are determined (number of cigarettes/day, pack years of smoking, ex-smoker status). Sputum is sampled (using suitable techniques) and rheology is assessed by means of a rotational-oscillatory rheometer (coaxial cylinders), tack test, and spin test for viscosity-elasticity, adhesivity, and spinnability, respectively. Smoking habits are correlated with rheology, and ciliary beat frequency is assessed in vitro on bronchial ciliated cells.

Results to Date:
A clear-cut separation was shown between sputum rheological properties of smokers and nonsmokers and also (although less evident) between smoking and nonsmoking chronic bronchitics. Smokers with chronic bronchitis also had the worst ciliary beat frequency (observed in vitro on bronchial ciliated cells).

Future Plans:
Assessment will be made of mucociliary transport rate in vitro on ciliated models (frog palate), with sputum from smokers and nonsmokers with/without chronic bronchitis and, in vivo, filming mucociliary transport of markers under special conditions (tracheostomized patients).

Project Dates:
November 1982–November 1986.

Financial Support:
Instituto Mallattie Respiratorie Dell' Universita, Milano; Town Council of Milan, Italy.

0324. ISTITUTO NAZIONALE PER LA RICERCA SUL CANCRO, Via le Benedetto XV, 10, 16132 Genoa, Italy.

Project Title:
Electrophysiological Concomitants of the Long-Term Withdrawal From Cigarette Smoking. A Pilot Study.

Principal Investigators:
Badellino, F.; Sannita, W.G.; Morasso, G., et al.

Objective:
To investigate electrophysiological changes (conventional and quantitative EEG; visual evoked potentials; contingent negative variation) occurring during long-term withdrawal from cigarette smoking.

Methods or Approach:
The 23 volunteers were requested to reduce smoking gradually over a 3-month period. Electrophysiological changes were recorded at monthly intervals.

Results to Date:
Definite EEG abnormalities were detectable on visual inspection in seven subjects at the beginning of the study (relative to nicotine plasma level above 70 ng/mL). Control measures during withdrawal were possible in only six subjects, due to limited compliance. In three of the six who stopped smoking abruptly, relevant EEG abnormalities appeared in conventional tracings during withdrawal. Systematic changes were not observed at quantitative EEG analysis, with the exception of significant variations in the right to left ratio of signal amplitude. A trend towards increase was observed in latency of late components of the visual evoked potentials, while contingent negative variation was not modified. Occurrence of EEG abnormalities during withdrawal has possible clinical relevance in the EEG routine.

Project Dates:
December 1983–December 1984.

Financial Support:
Istituto Nazionale per la Ricerca sul Cancro.

0325. ISTITUTO NAZIONALE PER LA RICERCA SUL CANCRO, Via le Benedetto XV, 10, 16132 Genoa, Italy.

Project Title:
Evaluation of Variations in the Psychologic and Psychophysiologic Parameters During and After Smoking Cessation.

Principal Investigators:
Morasso, G.; Crotti, N.; Lagomarsino, L.

Objective:
To clarify data obtained from a pilot project on patients who volunteered to follow a smoking cessation program.

Methods or Approach:
Routine interviews and tests were used to analyze personality changes (hypochondria, sensibility, resistance to stress, depression). Adjustments in personality were determined by MMPI retest and postcessation interviews.

Results to Date:
Preliminary results show that in patients in whom depression is not a relevant personality characteristic and where there is an increase in characteristics of hypochondria with risk of hysteria, anxiety acts as an interpersonal factor, reducing responses and the threshold of resistance to frustration and stress. About 70 percent of patients have undergone conjugal separation or perceive a threat of separation.

Future Plans:
Changes will be analyzed for stages of adjustment and personal consumption characteristics (mechanisms of habit and support) that recur in persons who voluntarily attempt to quit smoking.

Project Dates:
January 1984–continuing.

Financial Support:
Instituto Nazionale per la Ricerca Sul Cancro.

0326. ISTITUTO NAZIONALE PER LO STUDIO A LA CURA DEI TUMORI, Via Venezian, 20133 Milano, Italy.

Project Title:
Diet and the Risk of Lung Cancer in Females.

Principal Investigators:
Pastorino, U.; Berrino, F.; Valente, et al.

Objective:
To evaluate as potential risk factors for female lung cancer (1) dietary level of vitamins A and E and fats; (2) serum values of retinol, β-carotene, vitamins B_2, C and E, cholesterol, triglycerides, and lipoproteins; and (3) active and passive smoking.

Methods or Approach:
The study is restricted to a female population, where the etiologic role of tobacco is expected to be of minor importance. By the end of 1985, 100 consecutive patients with clinical diagnosis of lung cancer are expected to have entered the study. The control group will consist of 200 consecutive patients admitted to another research institute for nonneoplastic disease. A blood sample will be taken and all subjects will be interviewed regarding dietary and smoking habits. Relative risks among quartiles will be computed according to the Mantel-Haenszel method; attributable risk will be calculated by Miettiman's method.

Results to Date:
Preliminary analyses (30 cases, 129 controls) appear to confirm the negative relationship between dietary intake of vitamin A (both fractions) and risk of lung cancer. For serum values, no difference is evident for retinol, whereas a slight difference appears for β-carotene, which remains to be confirmed. Attributable risk for tobacco is about 25 percent.

Project Dates:
January 1982–December 1985.

Financial Support:
Istituto Nazionale per lo Studio e la Cura dei Tumori.

0327. ISTITUTO NAZIONALE TUMORI (National Cancer Institute), Venezian 1, 20133 Milan, Italy.

Project Title:
Proportion of Lung Cancer Cases Attributable to Occupational Exposure and Cigarette Smoking.

Principal Investigators:
Pastorino, U.; Berrino, F.

Objective:
To evaluate the increase of lung cancer risk in an unselected population according to (1) tobacco consumption (daily, total, duration, abstention); (2) occupational exposure to known carcinogens (length, latency, extent); (3) clinical features (cell type, site of tumor); and (4) estimation of the proportion of tumors attributable to smoking, occupational exposure, and their combined actions.

Methods or Approach:
A total of 204 lung cancer cases, all male, and 351 controls were studied. All cases occurred in a small geographic area between 1976 and 1979. Controls were extracted from the general population and matched by age and residence. All were interviewed for smoking habits and occupational histories. Relative standardized risks were computed by Mantel-Haenszel method; relative and attributable risks by the Miettinens.

Results to Date:
Overall relative risk for tobacco consumption (standardized by age and occupational exposure) was 7.0, and for occupational exposure (standardized by age and tobacco use) was 2.07. Risk attributable to tobacco consumption was 81 percent, to occupation 33 percent; for both, 89 percent. A multiplicative effect was evident between smoking and occupational exposure. For smoking, a linear trend was seen for amount smoked daily and number of years of consumption, and an inverse trend for ex-smokers by years of abstinence.

Project Dates:
January 1978–1983.

Reference:
Pastorino, U.; Berrino, R.; Gervasio, A., et al. "Proportion of Lung Cancers Due to Occupational Exposure." *International Journal of Cancer* 33:231-237, 1984.

0328. L. SACCO HOSPITAL, Servizio Fisiopatologia Respiratoria, Via G.B. Grassi 74, 20157 Milano, Italy.

Project Title:
Pulmonary Function in Adolescents, Healthy Smokers.

Principal Investigators:
Bosisio, E.; Sergi, M.; Manetti, M.

Objective:
To detect early smoking-induced alterations in ventilatory function (spirographic values, peak-flow, flow at 75, 50, and 25 percent of forced expiratory volume); diffusing capacity (transfer factor, single breath) and its components, D_m (diffusing capacity of alveolar capillary membrane); and V_c (volume of blood in the alveolar capillaries).

Methods or Approach:
Two groups of smokers, adolescents aged 14 to 16 years and 16 to 18 years, of both sexes will be studied. Subjects having a history of cardiopulmonary disease, cough, sputum, or acute respiratory disease during the last 3 months will be excluded. The behavior and social and economic status of subjects will be taken into account.

Results to Date:
Preliminary data on 16 subjects indicate that transfer factor, DM, ratio transfer factor/VA' (where VA' is the alveolar volume obtained through dilution of He during single breath test) decreased significantly, while Vc increased significantly. Data are in contrast with results obtained in smokers aged 25 to 30 years, where Vc did not vary.

Project Dates:
October 1982–February 1986.

Financial Support:
L. Sacco Hospital.

0329. L. SACCO HOSPITAL, Servizio Fisiopatologia Respiratoria, Via G.B. Grassi 74, 20157 Milan, Italy.

Project Title:
Transit Time Analysis of the Forced Expiratory Spirogram in Healthy Smokers After Exposure to H_2O Mist.

Principal Investigators:
Sergi, M.; Raguso, E.; Rizzi, M., et al.

Objective:
To study mean transit time, standard deviation and coefficient of variance of mean transit time, skewness, and index of skewness to detect modification of small airways in smokers.

Methods or Approach:
Smokers and nonsmokers (20 to 30 years of age) without sign of cardiopulmonary disease, will be studied before and after exposure to H_2O mist (10 min, 4 mL/min). The forced expiratory curve was divided into intervals of 0.2 sec, and volume of air exhaled during each interval was assigned a transit time (from beginning of expiration to time of appearance of the segment at the mouth). Mean transit time, standard deviation of transit time, coefficient of variance, skewness of transit time, and index of skewness will be calculated.

Results to Date:
Project is in a preliminary phase.

Project Dates:
December 1984–January 1986.

Financial Support:
L. Sacco Hospital, Milan, Italy.

0330. LEGA ITALIANA PER LA LOTTA CONTRO I TUMORI, Via Torlonia 15, Rome, Italy.

Project Title:
An Experimental Programme of Antismoking Education in Secondary Schools in Italy.

Principal Investigators:
Modolo, M.A.; Figa-Talamanca, I.
Objective:
To evaluate alternative educational approaches to antismoking education in secondary schools.
Methods or Approach:
The project, carried out in five cities, involves (1) baseline study (pretest) of knowledge, attitudes, and smoking habits of adolescents; (2) educational intervention, consisting in some schools of lectures, discussion, and self-survey and in other schools of addition of respiratory function tests for students and participating teachers; and (3) posttest 1 year later to measure changes in knowledge, attitudes, and smoking habits. One group of schools, which will receive only the pretest and posttest, will serve as a control group.
Results to Date:
A previous pilot study using the same design showed that respiratory function testing is a more effective instructional method, in that it involves each student personally and provides immediate feedback on respiratory impairment in smokers. The present study will determine the effectiveness of the method.
Future Plans:
If the respiratory function test provides considerably better results in terms of reducing smoking in adolescents, the method will be extended to large scale educational projects in schools.
Project Dates:
October 1984–June 1986.
Financial Support:
Lega Italiana per la Lotta Contro i Tumori.

0331. MARIO NEGRI INSTITUTE FOR PHARMACOLOGICAL RESEARCH, Via Eritrea 62, 20157 Milan, Italy. UNIVERSITY OF MILAN, Institute of Medical Statistics, Milan, Italy.

Project Title:
Patterns of Smoking Habits and Descriptive Epidemiology of Tobacco-Related Disease in Italy.

Principal Investigators:
La Vecchia, C.; Decarli, A.
Objective:
To (1) analyze trends in tobacco and cigarette sales (from 1900) and smoking (from 1950) in Italy as a whole and in various geographical areas by sex and age; (2) measure tar, nicotine, and carbon monoxide yields and market shares of various brands of Italian cigarettes; (3) analyze trends in mortality from lung cancer, other tobacco-related cancer, and cardiovascular and cerebrovascular disease (from 1955), and trends in various areas from 1970; and (4) analyze data for intranational and international comparisons.
Methods or Approach:
Trends in tobacco consumption are estimated from published and unpublished data of the State Monopoly, the Central Institute of Statistics, and Departments of Health and Finance. The major problem is establishing a reasonable estimate of smuggling. Measures of tar, nicotine, and carbon monoxide yields are commissioned to the British Laboratory of the Government Chemist and performed according to standard methods of analysis. Mortality rates are derived from publications and copies of original computer tapes obtained from the Central Institute of Statistics (with extracts of all primary death records). Analysis of mortality rates is based on a cross-sectional approach (age-specific and age-standardized rates, with major attention focused on younger age groups) and a cohort method.
Results to Date:
Cigarette consumption has increased steadily throughout this century in Italy. Trends showed particularly marked increases in three periods: in the 1920s, 1950s (possibly because of the spread of smoking among males following the two World Wars), and the 1970s (at least in part because of diffusion of smoking among women). In 1980, it was estimated that 54 percent of males and 17 percent of females were current smokers (9.9 percent and 1.4 percent ex-smokers, respectively). Lung cancer mortality has increased sharply in males over the last 30 years. In the late 1970s, lung cancer mortality in young and middle-aged men (35 to 44 and 45 to 54 years of age) was higher than in most other western countries. Rates for other tobacco-related cancers (esophagus, larynx, pancreas, kidney, and bladder) also increased, and were major determinants of the increasing cancer mortality in Italian men. When tobacco-related cancers were excluded from analysis, total cancer certification rates were decreasing slightly in both sexes up to age 64.
Project Dates:
January 1984–December 1988.
Financial Support:
Italian National Research Council (82.020.38.56; 82.020.45.56); Italian Association for Cancer Research, Milan; Italian League Against Cancer, Milan.

0332. MARIO NEGRI INSTITUTE FOR PHARMACOLOGICAL RESEARCH, Via Eritrea 62, 20157 Milan, Italy. UNIVERSITY OF MILAN, Institute of Medical Statistics, Milan, Italy.

Project Title:
Case–Control Surveillance of Neoplastic Disease.

Principal Investigators:
La Vecchia, C.; Decarli, A.
Objective:
To analyze and quantify cancer risk associated with cigarette smoking.
Methods or Approach:
Since 1979, case–control studies have been conducted with cancer patients and patients admitted for other acute conditions (controls) to university and general hospitals in the Milan area. A standard questionnaire is used to obtain information on smoking habits and other variables of interest. Cases (approximate number interviewed each year shown in parentheses) include patients admitted with histologically confirmed primary diagnosis of benign (150) and malignant (350) breast disease; benign (50) and malignant (50) ovarian cancer; cancers of the corpus (80); cancer of the esophagus (50); and cancer of the liver, gallbladder, and bile ducts (50). Controls are patients with acute, non-neoplastic disease, diagnosed within the year prior to interview. About 500 controls are interviewed each year. For each study, a file is created containing a determined number of controls for each case, selected at random (usually within strata of age and sex). Standard statistical methods are used for analysis.
Results to Date:
To date, data show a positive association between cigarette smoking and risk of cervical intraepithelial cancer and invasive

cervical cancer that is not totally explainable in terms of confounding. Also, smoking is postively associated with trophoblastic tumors; however, no relationship was found between smoking and cancer of the breast. Data are insufficient for evaluation of other cancers.

Project Dates:
March 1979–January 1988.

Financial Support:
Italian National Research Council (82.020.38.56, 82.020.45.56); Italian Association for Cancer Research, Milan.

0333. NATIONAL BOARD OF ELECTRICITY, MEDICAL SERVICE, ENEL - Git Tavazzano, Via Emilia, 20080 Tavazzano, Italy.

Project Title:
Relative Importance of Smoking and Occupational Pollutants on Lung Function of Power-Station Workers.

Principal Investigator:
Maroni, M.

Objective:
To evaluate relative importance of smoking and other polluting agents present in the working environment as risk factors for development of pulmonary function modifications; assess synergistic effects of smoking and exposure to dust and mineral fibers or welding fumes.

Methods or Approach:
The 350 workers at a thermoelectrical plant (fossil fuel) were studied using a specific questionnaire, clinical examination, and execution of pulmonary function tests at a 4-year interval. Results are analyzed comparing results in each worker after 4 years (prospective study) and comparing different groups of workers at each examination.

Results to Date:
Results are not yet available.

Project Dates:
January 1980–December 1985.

Financial Support:
National Board of Electricity, Italy.

0334. NATIONAL INSTITUTE ON CANCER RESEARCH, Via le Benedetto XV, 10, 16132 Genoa, Italy.

Project Title:
A Health Education Program, for Military Personnel, on the Hazards of Smoking.

Principal Investigators:
Arciti, C.; Mina, G.; Santi, L.

Objective:
To inform enlisted personnel concerning the hazards associated with smoking; attempt to reduce or eliminate cigarette consumption.

Methods or Approach:
In the two-part project, the first part is directed toward officers through conferences, audiovisual aids, and debates, to obtain a group that can inform soldiers on the hazards of smoking and that can act as effective role models. The second part is directed toward soldiers, through distribution of posters, pamphlets, booklets, and questionnaires to ascertain smoking habits. The program will be initiated in one region of Italy (Liguria) and will thereafter be extended to the rest of the country.

Results to Date:
Project is in a preliminary phase.

Project Dates:
January 1985–December 1988.

Financial Support:
National Institute on Cancer Research, Italy.

0335. NATIONAL INSTITUTE ON CANCER RESEARCH, Via le Benedetto XV, 10, 16132 Genoa, Italy.

Project Title:
A Program to Evaluate the Smoking Habits of Health Professionals.

Principal Investigators:
Arciti, C.; Cagliani, F.; Bottaro, P., et al.

Objective:
To ascertain smoking habits of health professionals in the main hospital of Genoa; increase awareness of smoking hazards of all hospital workers to modify existing habits.

Methods or Approach:
Questionnaires will be used to evaluate habits and attitudes toward smoking. All hospital personnel will also receive a booklet that explains the hazards of smoking and underlines the importance of medical doctors as educational role models. An estimated 5,000 people will participate.

Results to Date:
Project is in a preliminary phase.

Project Dates:
January 1985–December 1985.

Financial Support:
National Institute on Cancer Research, Italy.

0336. NATIONAL INSTITUTE ON CANCER RESEARCH, Via le Benedetto XV, 10, 16132 Genoa, Italy.

Project Title:
Smoking Education Campaign in Schools of the Genoa District.

Principal Investigators:
Santi, L.; Arciti, C.

Objective:
To (1) investigate smoking habits and effects of peer pressure and family influences on cigarette use among 10- to 18-year-old pupils in 200 schools in the Genoa district; (2) evaluate effectiveness of an educational program to prevent smoking; and (3) evaluate changes in smoking over time.

Methods or Approach:
The main intervention consists of organizing meetings and seminars for teachers, parents, and school doctors concerning cancer prevention and the dangers of smoking, and distributing guides for teachers and students and kits for experiments. A filmstrip, slides, and classroom reports are presented and debates and discussions are held with a group of students. Questionnaires are sent out at regular intervals for evaluating the learning rate of students, possible changes in habits, and quality of family involvement.

Results to Date:
Results of the antismoking program were very positive, particularly participation of individual students. Initially, the program was attended by small groups of interested students, but now includes over 15,000. Responses to the third questionnaire by 3,450 students showed that 255 (33 percent) of baseline smokers had quit and only 3 percent of students in the program had started to smoke compared with 17 percent among a control group. Results for teachers and doctors were

also positive; there was good participation and interest expressed during meetings.

Future Plans:

It has been proposed that the program be carried out on a national scale. Meanwhile, a predetermined subgroup of high school students will be followed from the time they enter high school until they graduate.

Project Dates:

September 1984–December 1988.

Financial Support:

National Institute on Cancer Research, Italy.

0337. UNIVERSITY OF GENOA, INSTITUTE OF HYGIENE, 1 Via Pastori, 16132 Genoa, Italy.

Project Title:

Effect of Cigarette Smoke on the Metabolic Activation/Deactivation of Mutagens by Human Lung Preparations.

Principal Investigators:

De Flora, S.; Giuntini, C.; Bartsch, H.

Objective:

To investigate metabolic activation of various procarcinogens, including unfractionated cigarette smoke condensate (CSC); (2) investigate deactivation of various direct-acting mutagens by preparations of human lung parenchyma and of the bronchial tree; and (3) evaluate interindividual variations and their possible sources, including smoking habits.

Methods or Approach:

Samples of peripheral lung parenchyma and bronchial tree tissue are collected, homogenized, and centrifuged at the University of Pisa. Corresponding S-12 fractions are returned to the laboratory as blind samples. Their ability to activate procarcinogens or to decrease activity of direct-acting mutagens is evaluated with the Ames test. Various enzyme activities are also monitored.

Results to Date:

None of the 69 preparations tested to date activated CSC to mutagenic metabolites; however, they were found to influence metabolic activation or deactivation of other mutagens.

Future Plans:

Additional samples are being tested. When completed, statistical analysis will be used to evaluate influence of smoking habits.

Project Dates:

January 1981–December 1986.

Financial Support:

Italian National Research Council.

0338. UNIVERSITY OF GENOA, INSTITUTE OF HYGIENE, 1 Via Pastore, 16132 Genoa, Italy.

Project Title:

Metabolic Effects of Cigarette Smoke in Pulmonary Alveolar Macrophages (PAM).

Principal Investigator:

De Flora, S.

Objective:

To investigate effects of smoking on biochemical activity in pulmonary alveolar macrophages (PAMs), including reduction of chromium mutagenicity and activity of various enzymes (e.g., DT-diaphorase, G6PD, 6PGD).

Methods or Approach:

PAMs are obtained from humans and rats by bronchoalveolar lavage. PAM homogenates or their subfractions are checked for various metabolic parameters. Decrease of Cr(VI) mutagenicity is evaluated in the Ames test.

Results to Date:

PAM homogenates and their fractions (especially cytosolic fractions) were found to be quite efficient in reducing Cr(VI). The underlying biochemical mechanisms are under investigation. There is some preliminary indication that this process, and some enzyme activity levels, are enhanced in PAMs of smokers, at least in individuals who smoke shortly before PAMs are collected.

Project Dates:

June 1984–December 1985.

0339. UNIVERSITY OF GENOA, INSTITUTE OF HYGIENE, 1 Via Pastore, 16132 Genoa, Italy.

Project Title:

Effects of Thiols on the Activation of Cigarette Smoke Condensate (CSC) to Mutagenic Metabolites.

Principal Investigator:

De Flora, S.

Objective:

To investigate effects of in vitro addition or in vivo treatment with thiols on metabolic activation of procarcinogens, including cigarette smoke condensate (CSC), or deactivation of direct-acting mutagens by rodent liver and lung preparations.

Methods or Approach:

Unfractionated CSC (and other mutagens) are assayed for mutagenicity in the Ames revertant test (*Salmonella*), in the presence of rat liver S-12 fractions supplemented with N-acetylcysteine (NAC, in vitro study), or of liver and lung S-12 fractions from rats pretreated with NAC, in various combinations with enzyme inducers (Aroclor 1254, phenobarbital, 3-methylcholanthrene) and glutathione (GSH) depletors (diethyl maleate, buthionine sulfoximine), in the in vitro study.

Results to Date:

In vitro addition of NAC had a diphasic effect on mutagenicity of CSC and other procarcinogens including (1) enhancement of S-9 mediated mutagenicity at intermediate NAC doses (ascribed to stimulation of activating metabolic pathways) and (2) complete loss of mutagenicity at high NAC doses (ascribed to trapping of electrophilic metabolites). Similar conclusions were drawn in the in vivo study. Under all conditions, mutagenicity of direct-acting mutagens was decreased by NAC.

Future Plans:

Research will investigate biochemical parameters involved in GSH metabolism and in biotransformation of carcinogens by liver and lung preparations of rats exposed to cigarette smoke and/or treated with NAC.

Project Dates:

June 1983–June 1986.

Financial Support:

Italian National Research Council.

Reference:

De Flora, S.; Bennicelli, C.; Zanacchi, P., et al. "*In Vitro* Effects of N-Acetlcysteine on the Mutagenicity of Direct-Acting Compounds and Procarcinogens." *Carcinogenesis* 5(4):505-510, April 1984.

0340. UNIVERSITY OF MILAN, INSTITUTE OF OCCUPATIONAL HEALTH, Clinica del Lavoro "L. Devoto," 20122 Milano, Italy.

Project Title:

Influence of Smoking Habits on Microsomal Enzyme Induction.

Principal Investigators:

Colombi, A.; Maroni, M.; Foa, V.

Objective:
To determine whether cigarette smoking can influence activity of hepatic microsomal enzymes in humans.

Methods or Approach:
The investigation was carried out on healthy subjects to evaluate the normal range of urinary D-glucaric acid (GLA) excretion and to assess the influence of sex, age, and smoking on urinary GLA excretion. GLA was measured on spot urine samples and results were evaluated. Mean age for males was 41 years (range 18 to 60); mean age for females was 35 years (range 19 to 54).

Results to Date:
Among the 402 males, 36 percent were nonsmokers, 40 percent smoked ≤ 19 cigarettes/day, and 24 percent smoked a pack or more/day. Proportions for the 171 females were 62 percent nonsmokers and 38 percent smokers. A highly significant increase in urinary GLA excretion was observed in male smokers that was less evident in female smokers. Different reference values must be considered for smokers and nonsmokers when effects of environmental or occupational exposure to chemicals are evaluated by means of this test.

Project Dates:
January 1982–November 1982.

Financial Support:
University of Milan, Italy.

Reference:
Colombi, A.; Maroni, M.; Antonini, C., et al. "Influence of Sex, Age and Smoking Habits on the Urinary Excretion of D-Glucaric Acid." *Clinica Chemica Acta* 128:349-358, 1983.

0341. UNIVERSITY OF PERUGIA, HYGIENE AND PREVENTIVE MEDICINE INSTITUTE, Via del Giochetto, P. le Ruata, 06100 Perugia, Italy.

Project Title:
Hormonal Receptor Breast Cancer and Some Risk Factors. A Case–Control Study.

Principal Investigators:
Modolo, M.A.; Minelli, L.; Panella, V.

Objective:
To (1) establish the relative risk and the attributable risk of smoking in etiology of breast cancer in women from two different geographic areas of Italy; (2) evaluate possible activity of hair dyes (oxidative and nonoxidative products) in development of breast cancer; and (3) investigate whether a relationship exists between the presence of these two possible risk factors and the progestin and estrogen receptor status of cancer tissue.

Methods or Approach:
Cases with histological diagnosis of breast cancer complete questionnaires regarding smoking habits and hair dye use throughout life. Information is also obtained on socioeconomic status, chronic use of drugs, hormonal therapy, and other established risk factors for breast cancer. Two controls, matched for age and social class, will be selected for each case from other hospital wards, excluding women with cancer at any site and other gynecological disorders. Only women from Umbria and Emilia-Romagna (from 25 to 50 years of age) will be included.

Results to Date:
In a similar case–control study of women from Campania, no association between smoking and breast cancer was found (odds ratio 0.78).

Project Dates:
September 1985–December 1986.

Financial Support:
University of Perugia, Hygiene and Preventive Medicine Institute.

0342. UNIVERSITY OF PERUGIA, HYGIENE AND PREVENTIVE MEDICINE INSTITUTE, Via del Giochetto, 06100 Perugia, Italy.

Project Title:
Smoking Habits Among High School Students in Italy.

Principal Investigators:
Modolo, M.A.; Monarca, S.; Catanelli, M., et al.

Objective:
To (1) analyze trends in smoking habits of Perugia students for 1960, 1970, and 1980; (2) study smoking habits of high school students from sample schools in 10 Italian towns; (3) analyze correlations between use of tobacco, alcohol, and psychoactive medicines; (4) conduct followup after 6 years; and (5) evaluate effect of campaigns organized by the Italian League Against Cancer, schools, and other institutions.

Methods or Approach:
High school students aged 15 to 18 years from all schools in Perugia (approximately 2,000) and samplings of students from schools in 10 other towns (approximately 8,000) were interviewed using a 58-item anonymous questionnaire. Data was collected on smoking habits, knowledge of and attitudes toward smoking, alcohol consumption, and use of psychoactive medicines.

Results to Date:
Results for Perugia students have been reported. Data on students in the other towns show that (1) tobacco consumption was similar in the different towns; (2) age of first smoking attempt was earlier among 15-year-olds than among older students; (3) proportions of occasional or current smokers were higher among girls; 25 percent at age 15 (boys, 24 percent) and 47 percent at age 18 (boys, 42 percent); (4) smoking habits were statistically related to age, smoking habits of parents, siblings, and friends, age of smoking initiation, and attitudes of parents toward smoking by sons and daughters; (5) knowledge of tobacco-related problems was higher among nonsmokers than among smokers; (6) wine, the commonest form of alcohol used, is consumed by 16 to 41 percent of students; (7) 9 to 12 percent of students had used psychoactive drugs in the 12 months preceding the survey (higher use among females); and (8) smoking habits were strongly associated with alcohol consumption, and slightly associated with use of psychoactive drugs.

Future Plans:
A similar followup survey will be conducted in the future to ascertain trends in smoing habits The effect of a campaign against tobacco use will be evaluated.

Financial Support:
Italian Ministry of Health; Italian League Against Cancer.

0343. UNIVERSITY OF PERUGIA, INSTITUTE OF HYGIENE, Via del Giochetto, I-06100 Perugia, Italy.

Project Title:
Metabolism of Mutagens/Carcinogens Present in Cigarette Smoke: Enzymatic Induction, Activation, and Detoxification.

Principal Investigators:
Scasseliati Sforzolini, G.; Savino, A.; Monarca, S., et al.

Objective:
To (1) investigate induction of aryl hydrocarbon hydroxylase (AHH) and dimethylnitrosamine demethylase (DMND) activities in rat liver and lung tissues by mainstream and sidestream

smoke condensates and their fractions; (2) study activation and detoxification of mutagens present in smoke condensates; and (3) determine AHH and DMND activities in human lung tissues of smokers and nonsmokers.

Methods or Approach:

Mainstream and sidestream smoke condensates from 300 cigarettes were obtained from a smoking machine under standard conditions. Mainstream smoke was condensed in three serial traps cooled with liquid nitrogen, and sidestream smoke particulate matter was collected on filters with a high volume air sampler. Condensate and particulate matter were dissolved in acetone and extracts dried. Aliquots of extracts were stored, and the remaining portions were fractionated in six fractions: soluble bases, insoluble bases, soluble acids, insoluble acids, paraffin hydrocarbons, and polyaromatic hydrocarbons. Rats were injected i.p. with known inducers (Aroclor-1254, phenobarbital, benzo(*a*)pyrene, 3-methylcholanthrene) and with fractionated and unfractionated smoke condensates. Induction of AHH and DMND activities was determined in liver and lung homogenates obtained from treated rats using spectrophotometric and spectrophotofluorimetric methods and the Ames test.

Results to Date:

AHH responses observed in hepatic and pulmonary tissues following treatment of male rats with mainstream and sidestream cigarette smoke condensates and their fractions showed that soluble bases, insoluble bases, and polyaromatic hydrocarbons induce hepatic and pulmonary AHH activity. The Ames test appeared much less sensitive than the spectrophotofluorimetric method in detecting AHH induction.

Project Dates:

October 1984–September 1986.

Financial Support:

Italian National Research Council (84.00795).

0344. UNIVERSITY OF TORINO, Via Santena 7, 10126 Torino, Italy.

Project Title:

Case–Control Study of Cancer of the Urinary Tract in the Province of Turin, Italy.

Principal Investigators:

Terracini, B.; Vineis, P.

Objective:

To (1) establish the role (relative and attributable risks) of tobacco smoking, occupational exposures, and other agents in the etiology of cancer of the urinary tract in an industrial area of Northern Italy; (2) investigate whether the type of cigarettes (blond/black tobacco, filtered/unfiltered) is important in the association between tobacco and cancer of the urinary tract; and (3) explore the possibility of an interaction between tobacco smoking and other etiologic factors.

Methods or Approach:

Hospitalized cases of urinary tract cancer in the Province of Turin are interviewed with a standard questionnaire regarding smoking habits throughout life, full occupational history, coffee consumption, artificial sweetener use, and analgesic use. Each case is age- and sex-matched with a control from the same urological ward (excluding patients with cancer at any site, cystitis, and hematurias of unknown origin). Since 1981, controls have been recruited in surgical wards of the same hospital. In addition, a random sample of the population of the city of Torino is being interviewed and used as a second control group.

Results to Date:

By December 1981, 225 cases and 225 urological controls (males only) had been analyzed with regard to tobacco consumption and occupation. The overall relative risk for cigarette smokers was 4.8 (age-standardized). Relative risks for men smoking an average of 1-9, 10-19, 20-29, and 30+ cigarettes/day throughout life were, respectively, 2.5, 5.9, 7.0, and 7.8. The relative risk associated with occupations known to have an etiological role in cancer of the urinary tract (lasting at least 6 months in any life period) was 1. Relative risks determined by cigarette smoke were also estimated separately in persons occupationally exposed and nonoccupationally exposed. The comparison suggests a multiplicative effect.

Project Dates:

October 1977–1984.

Financial Support:

University of Turin; Regional Health Authority; Italian Association for Research on Cancer.

0345. UNIVERSITY OF TORINO, Chair of Cancer Epidemiology, Via Santena 7, 10126 Torino, Italy.

Project Title:

Cancer of the Oral Cavity and Oropharynx in the City of Torino, Italy.

Principal Investigators:

Merletti, F.; Terracini, B.; Mashberg, A.

Objective:

To (1) investigate association of alcohol, tobacco, and occupation with cancer of the oral cavity and oropharynx; (2) determine interaction of alcohol and tobacco in oral carcinogenesis in a population who drink heavily, but where a relatively large proportion of drinkers do not smoke; and (3) investigate effect of different beverages and of black and blond tobacco on oral carcinogenesis.

Methods or Approach:

The project is a population-based case–control study. New cases among residents of Torino and a random sample of the general population are being interviewed to establish lifetime occupational history and current and past use of tobacco and alcohol. As of November 1984, 110 cases and 300 controls had been interviewed.

Results to Date:

Results are not yet available.

Project Dates:

July 1982–December 1985.

Financial Support:

Ministry of Education, Italy; Italian Association for Research on Cancer.

0346. UNIVERSITY OF TORINO, Chair of Cancer Epidemiology, Via Santena 7, 10126 Torino, Italy.

Project Title:

Drinking and Smoking Habits in the General Population of Torino, Italy.

Principal Investigators:

Merletti, F.; Terracini, B.; Boffetta, P.

Objective:

To investigate temporal variations in drinking and smoking habits in the general population of Torino, Italy.

Methods or Approach:

A random sample of the population of Torino (approximately 1,200 persons) is being interviewed. The nutritional and occupational questionnaire being used includes items that detail smoking and alcohol consumption history.

Results to Date:

Results are not yet available.

Project Dates:
January 1979–December 1985.
Financial Support:
Centro Nazionale Ricerche, Italy; Italian Association for Research on Cancer.

0347. UNIVERSITY OF TORINO, CHAIR OF CANCER EPIDEMIOLOGY, Torino, Italy.

Project Title:
Epidemiological Investigation on Laryngeal Cancer.

Principal Investigators:
Terracini, B.; Merletti, F.; Tuyns, A.
Objective:
To investigate the association of alcohol, tobacco, and occupation with cancer of the larynx; determine effect of different types of beverages and of different types of tobacco (blond, black) in laryngeal carcinogenesis.
Methods or Approach:
A population-based case-control study will be conducted. A total of 330 cases (290 males and 40 females) have been interviewed to date.
Results to Date:
Results are not yet available.
Project Dates:
January 1979–December 1985.
Financial Support:
Centro Nazionale Ricerche, Italy; Italian Association for Research on Cancer.

0348. HOSPITAL OF MONFALCONE, Laboratory of Pathological Anatomy, 34074 Monfalcone, Italy.

Project Title:
Billroth II Gastric Resection and Lung Carcinoma.

Principal Investigators:
Bianchi, C.; Brollo, A.; Dittesini, L.
Objective:
To determine whether excess lung cancer in patients formerly subjected to Billroth II resection for benign conditions is primarily related to gastric resection, differences in smoking habits, or other factors.
Methods or Approach:
A series of consecutive necropsies will be analyzed. Prevalence of lung carcinoma among subject with previous Billroth II resection will be compared with that among controls chosen from the same series.
Results to Date:
Project is in a preliminary phase.
Project Dates:
December 1984–December 1985.
Financial Support:
Hospital of Monfalcone, Italy.

JAPAN

0349. AICHI CANCER CENTER HOSPITAL, Department of Pathology and Clinical Laboratories, Tashiro-cho, Kanokoden, Chikusa-ku, Nagoya, Japan 464. AICHI MEDICAL UNIVERSITY, INSTITUTE FOR MEDICAL SCIENCE OF AGING, Yazako, Nagakute-cho, Aichi-gun, Aichi, Japan 480-11.

Project Title:
So-called "Female Type" of Lung Cancer–Development, Growth, and Smoking Habits.

Principal Investigators:
Sato, T.; Tauchi, H.
Objective:
To determine relationship of histology, age, sex, and site of primary growth of so-called "female" and "male" types of lung cancer, with special reference to smoking habits of patients.
Methods or Approach:
Histological and electromicroscopic investigation is being conducted on 300 male and 109 female surgically resected lung cancer patients at the Aichi Cancer Center Hospital, 130 female cases in Hawaii, and 28 female cases at the Tokyo Metropolitan Geriatric Hospital.
Results to Date:
In Japan today, the majority of female lung cancer cases are of the "female" type that are not related to smoking; dominant histology was adenocarcinoma in the peripheral portion of the lung. Similar characteristics in age-adjusted relative risk associated with smoking habits were seen in male patients. In Hawaii and Toyko, the majority of female smokers showed squamous cell carcinoma similar to male cases.
Future Plans:
The carcinoembryonic antigen will be investigated by immunohistochemical methods and compared in male and female types of lung cancer. In addition, the relationship between carcinogenesis and lipid metabolism in the lung will be studied.
Project Dates:
April 1982–continuing.
Financial Support:
Aichi Cancer Center; Aichi Cancer Research Foundation; JTSPC.

0350. AICHI CANCER CENTER RESEARCH INSTITUTE, Kanokoden 81-1159, Tashiro-cho, Chikusa-ku, Nagoya, Japan 464.

Project Title:
Cigarette Smokers' Characteristics.

Principal Investigators:
Ogawa, H.; Tominaga, S.; Aoki, K.
Objective:
To elucidate the characteristics of cigarette smokers in terms of health conditions, food habits, personality, and social backgrounds.
Methods or Approach:
In 1970, approximately 16,000 male and female civil service employees of Nagoya city responded to a health screening questionnaire. The respondents were stratified by age and cigarette smoking habit, and about 25 percent of the samples (male adults) were selected systematically from each stratum. The linear dose-response relationship between the amount of cigarettes smoked and the response to specific questionnaire items was determined.
Results to Date:
It was shown by comparison between smokers, ex-smokers, and never smokers that smokers tended to be engaged more in

outdoor service, have a lower education, complain of subjective symptoms, be extroverted, prefer to eat sensory-stimulating foods, and drink coffee and alcohol. More intensive analysis of the association between smoking and subjective symptoms was performed and many were found to be in a dose–response relationship with smoking. Few sex differences were observed. Although the major objective of the study has been achieved, the cohort investigation is continuing.

Project Dates:
July 1977–continuing.

Financial Support:
Aichi Cancer Center Research Institute.

0351. AICHI CANCER CENTER RESEARCH INSTITUTE, Kanokoden 81-1159, Tashiro-cho, Chikusa-ku, Nagoya, Japan 464.

Project Title:
Japan and United States Comparative Study on Smoking Behavior Among Junior High School Students.

Principal Investigators:
Ogawa, H.; Aoki, K.; Gellert, G.

Objective:
To compare cigarette smoking among junior high school students in Japan and the United States, with reference to prevalence of smoking, motivational aspects of smoking, knowledge of the health hazards of smoking, and attitudes toward smoking.

Methods or Approach:
A self-administered questionnaire survey of almost 3,000 pupils in three junior high schools in Nagoya, Japan, was conducted in January 1981. The questionnaire included items on current smoking status; smoking among family members and intimate friends; estimation of proportions of smokers among school teachers, adults, and pupils; opinion on teenage smoking; and motivational aspects of smoking behavior. Many of these items had already been used in nationwide surveys on teenage smoking in the United States in 1974 and 1979. Survey results will be compared.

Results to Date:
Survey data are being analyzed.

Project Dates:
October 1981–1983.

Financial Support:
Aichi Cancer Center Research Institute.

0352. AICHI CANCER CENTER RESEARCH INSTITUTE, Division of Epidemiology, 81-1159 Kanokoden Tashiro-cho, Chikusa-ku, Nagoya, Japan 464.

Project Title:
Relationship Between Air Pollution and Lung Cancer in Japan.

Principal Investigators:
Tominaga, S.; Kuroishi, T.; Nakagawa, N.

Objective:
To clarify the relationship between air pollution and lung cancer mortality taking into consideration other factors such as smoking, availability of medical services, and socioeconomic factors.

Methods or Approach:
Correlation analyses were conducted to examine the relationship between the age-adjusted lung cancer mortality and the level of ambient air pollution (SO_2 level, NO_2 level), and other related factors including smoking and socioeconomic factors by prefecture.

Results to Date:
In males, the lung cancer mortality was not related to most factors considered in this study, but in females the lung cancer mortality was related to many factors including the level of air pollution, population density, and tobacco consumption. It is suggested that the positive relationship between the lung cancer mortality and the level of air pollution and several other factors in females was due to a greater proportion of female smokers in urban areas.

Future Plans:
Data collection (cancer mortality statistics and data on air pollution) will be continued and further analyses will be conducted.

Project Dates:
April 1977–1985.

Financial Support:
Aichi Cancer Center Research Institute; Ministry of Education, Japan.

0353. AICHI UNIVERSITY OF EDUCATION, Department of Health Science, Hirosawa-1, Igaya-cho, Kariya-city, Aichi, Japan 448.

Project Title:
A Study on the Image for Smoking Among the School Children and Students.

Principal Investigators:
Muramatsu, T.; Tanaka, T.; Muramatsu, S.

Objective:
To investigate the image of smoking among schoolchildren and students in Japan.

Methods or Approach:
Open-ended interviews were conducted with 881 schoolchildren and students living in two cities. Answers were grouped by category according to viewpoint expressed: (1) negative, (2) affirmative, (3) emotional, (4) physical, and (5) ethical.

Results to Date:
Responses were grouped into 58 categories; 70 percent of the categories reflect a negative view of smoking, 34.5 percent evaluate smoking from a physical viewpoint, 25.9 percent from an emotional viewpoint, and 29.3 percent from an ethical viewpoint. The most common response was that "Smoking is bad for the health." The next most common answers were that the children would not smoke as adults, that they disliked smoking, that it was bad smelling, annoying, harmful to people nearby, and the main cause of lung cancer. Among those surveyed, girls, elementary schoolchildren, and young people who live in large cities tended to reject smoking. To effectively carry out antismoking education for young people, emotional, ethical, and physical aspects of smoking must be considered. Other important considerations are sex, age, and locale.

Project Dates:
October 1982–December 1983.

Financial Support:
Aichi University of Education.

0354. CANCER INSTITUTE, Department of Experimental Pathology, 1-37-1 Kami-Ikebukuro, Toshima-ku, Tokyo, Japan 170.

Project Title:
Activation and Detoxification of Polycyclic Hydrocarbons Contained in Tobacco Condensate.

Principal Investigators:
Takayama, S.; Nemoto, N.

Objective:
To study the role of the activation and detoxification system in benzo(*a*)pyrene (BaP) carcinogenesis.
Methods or Approach:
Ingested BaP is metabolized to activated forms to induce tumors or excreted as inactivated forms. The enzyme system responsible for activation is a cytochrome P-450 system, which has been extensively studied. However, the other metabolic pathway (involving an oxidation by active oxygen) has recently been suggested in the activation of BaP. Correlation among the enzymes, including activation- and detoxification-related conjugase with glutathione, glucuronic acid, and sulfuric acid, will be investigated. Other factors that influence the biological activity of BaP will also be surveyed.
Results to Date:
Biological activities of BaP are influenced by various factors that lack enzyme activity (heme compounds, serum, unsaturated fatty acids). It was observed that BaP is activated to bind to cellular macromolecules, mediated by an arachidonic acid-dependent system. Findings suggest that polycyclic hydrocarbons are activated by prostaglandin synthetase or lipid peroxidase, in addition to the cytochrome P-450 system.
Future Plans:
Involvement of active oxygens for activation of polycyclic hydrocarbons will studied further.
Project Dates:
April 1984–March 1986.
Financial Support:
Japan Tobacco and Salt Public Corporation.

0355. CENTER FOR ADULT DISEASES, OSAKA, 1-3-3 Nakamichi, Higashinari-ku, Osaka, Japan 537.

Project Title:
Relationship of Smoking to Adenocarcinoma of Lung Cancer in the Female.

Principal Investigators:
Hanai, A.; Fujimoto, I.; Nakamura, M.
Objective:
To investigate the relationship of lung cancer and smoking in females.
Methods or Approach:
In the case–control study, lung cancer patients diagnosed at the Center for Adult Diseases, Osaka, are compared with controls selected from patients at the same hospital who are diagnosed as having cancer at sites other than the lung, matched by month of diagnosis, sex, and age. Questionnaires, which include items on smoking history, are completed by all patients on their first visit to the hospital. Data analyses have been completed for male patients, but the limited number of female smokers who are lung cancer patients makes it necessary to continue the study until an appropriate number of cases is accrued.
Results to Date:
Relative risk of smoking among males was found to be highest for small cell carcinoma, followed by squamous cell carcinoma, large cell carcinoma, and adenocarcinomas. All risks were statistically significant. A dose–response relationship by daily cigarette consumption and by smoking index was observed in all histological types except adenocarcinoma.
Future Plans:
A case–control study, utilizing interviews is being planned to investigate the relationship between passive smoking and other Japanese lifestyle factors and lung cancer.
Project Dates:
April 1983–December 1986.
Financial Support:
Japanese Ministry of Education.

0356. CENTRAL INSTITUTE FOR EXPERIMENTAL ANIMALS, Preclinical Research Laboratories, 1433 Nogawa, Miyamae-ku, Kawasaki, Japan 213.

Project Title:
Psychopharmacological Factors of Smoking Studied in Rhesus Monkeys.

Principal Investigators:
Yanagita, T.; Ando, K.; Kato, S.
Objective:
To (1) observe influences of unit dose changes on daily intake in intravenous self-administration of nicotine; (2) establish smoking behavior by using aversive stimulus; and (3) observe influence of voluntary smoking on conflict behavior.
Methods or Approach:
Monkeys were allowed to take nicotine at different unit doses (4, 15, 60, 120, 240 μg/kg) at 2 weeks/unit dose under a continuous procedure. Daily intake rates were observed. Monkeys were trained to smoke cigarettes to avoid electric shock, using the Sidman avoidance schedule. Voluntarily smoking monkeys were subjected to a situation where licking water was accompanied by electric schock, and frequency of licking with shock was compared during the smoking-available period and the air-sucking control period.
Results to Date:
There was little change in daily intake rates as the unit dose was changed within a range below 240 μg/kg. Stable and frequent voluntary smoking behavior was maintained under the nonshock extinction condition in most monkeys. When smoking became available following stabilizing of licking, licking first decreased and then increased. When smoking was deprived, licking increased in one monkey and decreased in one other.
Future Plans:
Experiments will be continued and the influences of smoking on lever-pressing conflict behavior will be investigated.
Project Dates:
April 1982–March 1986.
Financial Support:
Japan Tobacco and Salt Public Corporation.

0357. CENTRAL INSTITUTE FOR EXPERIMENTAL ANIMALS, Preclinical Research Laboratories, 1433 Nogawa, Miyamae-ku, Kawasaki, Japan 213.

Project Title:
Interaction Between Smoking and Psychotropic Substances.

Principal Investigators:
Yanagita, T.; Ando, K.; Iizuka, H.
Objective:
To observe the influence of psychotropic substances on the pharmacological effects of smoking and on smoking behavior.
Methods or Approach:
Interaction was studied in rats utilizing (1) nicotine (0.5 mg/kg, s.c.) and either diazepam (1 to 128 mg/kg, p.o.) or *d*-amphetamine (0.6 to 2 mg/kg, s.c.), and *d*-amphetamine (0.5 mg/kg, s.c.) and diazepam (1 to 128 mg/kg, s.c.) in a DRL 20-sec experiment; (2) nicotine (0.1 mg/kg, s.c.) and diazepam (0.1 mg/kg, p.o.), to examine fighting behavior induced by electric stimulation; (3) nicotine (0.5 mg/kg, s.c.) and either *d*-amphetamine (1.4 mg/kg, s.c.) or apomorphine (0.6 to 1 mg/kg, s.c.), to examine stereotypy; and (4) nicotine (0.02 or 0.04 mg/kg, i.v.) and chlorpromazine (1.0 mg/kg, s.c.) to

examine EEG effects. In addition, the influence of ethanol (2.0 g/kg, p.o.) on intravenous self-administration of nicotine was studied by a progressive ratio test in rhesus monkeys.

Results to Date:

Diazepam and *d*-amphetamine enhanced the effect of nicotine to shorten IRTs. Diazepam also enhanced the effect of *d*-amphetamine. The suppressive effect of nicotine was converted to a stimulative effect by diazepam pretreatment. Nicotine enhanced the effect of *d*-amphetamine but not of apomorphine, antagonized the depressive effect of chlorpromazine on the cortex, and enhanced the effect of chlorpromazine on the hypocampus. Ethanol weakened the reinforcing effect of nicotine, with one exception in which the effect was markedly enhanced.

Future Plans:

Other psychotropic drugs will be added to experiments with rats and the influence of psychotropic drugs on smoking behavior in rhesus monkeys will be studied.

Project Dates:

April 1982–March 1986.

Financial Support:

Japan Tobacco and Salt Public Corporation.

0358. CHIBA UNIVERSITY, SCHOOL OF MEDICINE, Institute of Pulmonary Cancer Research, 1-8-1 Inohana, Chiba, Japan 280.

Project Title:

Co-Carcinogenic Effect of Asbestos and Cigarette Smoking.

Principal Investigators:

Kimizuka, G.; Hayashi, Y.

Objective:

To determine cocarcinogenic effect of cigarette smoking during exposure to asbestos.

Methods or Approach:

Asbestos fibers (UICC chrysotile B) were injected into hamsters intratracheally with and without benzo(*a*)pyrene (BaP). Animals were sacrificed at certain endpoints. Hamsters were also exposed to cigarette smoke for 10 min, twice/day, 4 days/week, following two asbestos injections.

Results to Date:

Epithelial hyperplasia and metaplasia of airways (probably peripheral) were severe and more frequent in lungs of hamsters that received both asbestos and BaP than in animals injected with either asbestos or BaP alone. Squamous metaplasia with keratinization was also found in lesions of hamsters injected with both asbestos and BaP.

Future Plans:

The effect of asbestos with/without BaP in carcinogenesis of the lung will be investigated.

Project Dates:

September 1982–continuing.

Financial Support:

Chiba University, Japan.

0359. DAICEL CHEMICAL INDUSTRIES LTD., No. 1, Teppo-cho, Sakai, Osaka, Japan 590.

Project Title:

New Plasticizers and New Additives for Cigarette Filters.

Principal Investigators:

Sawada, H.; Kawamoto, J.; Shiga, M., et al.

Objective:

To develop new nontoxic plasticizers that harden cigarette filter rods rapidly; develop new additives that remove harmful compounds from cigarette smoke.

Methods or Approach:

Gas chromatography and liquid chromatography have been employed to determine harmful compounds in cigarette smoke.

Results to Date:

New plasticizers such as E-caprolactam and methyl ethers have been developed that harden filter rods more rapidly than triacetin.

Project Dates:

January 1985–December 1986.

Financial Support:

Daicel Chemical Industries Ltd. (Japan).

0360. DEPARTMENT OF PUBLIC HEALTH, JICHI MEDICAL SCHOOL, Yakushiji Minamikawachi-machi, Tochigi-ken, Japan 329-04.

Project Title:

A Study of the Factors Associated With Low Birth Weight. A Case–Control Study in Tochigi Prefecture.

Principal Investigators:

Nagai, M.; Yanagawa, H.; Kawaguchi, T., et al.

Objective:

To identify and evaluate risk factors for low birth weight infants including smoking habits of parents.

Methods or Approach:

Cases were all low birth weight infants (≤ 2500 g) born in Tochigi prefecture between June 1, 1982, and December 31, 1982. One control infant was matched with each case for sex, birthplace, and birth date (within 2 months). Public health nurses visited mothers to collect background and pregnancy data (family and mother's pregnancy history, parents' height, weight, income, and smoking and drinking habits).

Results to Date:

Factors related to low birth weight were age (too young or too old), first pregnancy, more than two stillbirths, lower birth weight of older siblings, small stature and weight of mother, fewer examinations during pregnancy, and smoking by mother or father.

Project Dates:

April 1982–December 1984.

Financial Support:

Tochigi Prefecture Government.

Reference:

Nagai, M.; Yanagawa, H. "A Study of the Factors Associated With Low Birth Weight. A Case–Control Study in Tochigi Prefecture." *Journal of Child Health* 43(6), 1984 (Japanese) (In press).

0361. ENVIRONMENTAL POLLUTION CONTROL CENTER, 62-3, 1 Chome, Nakamichi, Higashinari-ku, Osaka City, Japan 537.

Project Title:

Chromatographic Determination of Aldehydes in Polluted Air or Gas Sample.

Principal Investigators:

Kuwata, K.; Uebori, M.; Tanaka, S.

Objective:

To develop rapid, simple analytical methods for determining traces of aromatic and aliphatic aldehydes in polluted air (including tobacco smoke) that provide accurate determination of traces of these compounds without interfering effects.

Methods or Approach:

Traces of C_1-C_4 alkylaldehydes and benzaldehyde in air are trapped, using Sep-PAK C_{18} impregnated with 2,4-dinitrophenylhydrazine and phosphoric acid, and analyzed for derivation products by high performance liquid chromatography. The analytical column used is packed with Develosile ODS-3 (3 µm) and the mobile phase is 65/33 acetonitrile/water.

Results to Date:
Methods are examined with respect to fundamentals and applications. The derivatives of the aldehydes are completely separated without interfering effects of other organic substances. Aldehydes in air are accurately determined at ppm or ppb levels; detection limits are 0.2-1.0 ppb/100 L. A large number of polluted air samples (ambient air, auto exhaust, industrial emissions, tobacco smoke) were analyzed.

Future Plans:
More convenient methods for determining traces of aldehydes are being developed and will be used for environmental research.

Project Dates:
April 1982–March 1985.

Financial Support:
Environmental Pollution Control Center, Japan.

References:
(1) Kuwata, K.; Uebori, M.; Yamasaki, Y. "Determination of Aliphatic and Aromatic Aldehydes in Polluted Airs as Their 2,4-Dinitrophenylhydrazones by High Performance Liquid Chromatography." *Journal of Chromatographic Science* 17:264-268, May 1979. (2) Kuwata, K.; Uebori, M.; Yamasaki, H., et al. "Determination of Aliphatic Aldehydes in Air by Liquid Chromatography." *Analytical Chemistry* 55(12):2013-2016, October 1983.

0362. ENVIRONMENTAL POLLUTION CONTROL CENTER, 62-3, 1 Chome, Nakamichi, Higashinari-ku, Osaka City, Japan 537.

Project Title:
Chromatographic Determination of Alkylamines and Alkylthiols in Gas Samples.

Principal Investigators:
Kuwata, K.; Nishikawa, Y.; Akiyama, E.

Objective:
To develop analytical techniques for determining traces of alkylamines and alkylthiols at ppb levels in polluted air (including tobacco smoke).

Methods or Approach:
Traces of C_1-C_4 alkylamines in air were collected using Sep-Pak C_{18} impregnated with phosphoric acid, and absorbed materials were removed with methoanol/water (1:1). The eluate, adjusted to pH 10, was analyzed by gas chromatography. The analytical column was packed with SEPABEAD GHP-1 (60-80 mesh). Absorbed materials were removed and amine derivatives were determined. Traces of C_1-C_4 alkylthiols in air were collected using Sep-Pak Florisile impregnated with NBD-Cl; resulting derivatives were removed with methanol and determined with fluorescent detection. The analytical column used was packed with Develosile ODS-3; the mobile phase was 45/55 acetonitrile/water.

Results to Date:
Amines and thiols could be accurately determined at pmole levels without interference by other organic substances. Detection limits of the C_1-C_4 alkylamines and the C_1-C_4 alkylthiols were 0.1-24.0 pmole and 3.1-69.0 pmole, respectively. A large number of polluted air samples were analyzed.

Future Plans:
More convenient methods for determining traces of the compounds are being developed and will be used for environmental research.

Project Dates:
April 1981–March 1985.

Financial Support:
Environmental Pollution Control Center, Japan.

Reference:
Nishikawa, Y.; Kuwata, K. "Liquid Chromatographic Determination of Low Molecular Weight Aliphatic Amines in Air via Derivatization With 7-Chloro-4-Nitro-2,1,3-benzoxadiazole." *Analytical Chemistry* 56(11):1790-1793, September 1984.

0363. FUJITA-GAKUEN HEALTH UNIVERSITY, COLLEGE OF MEDICAL TECHNOLOGY, Toyoake City, Aichi, Japan 470-11.

Project Title:
The Effect of Cigarette Smoking on Lung Function.

Principal Investigators:
Nagashima, T.; Umeda, H.

Objective:
To investigate acute and chronic effects of cigarette smoking on peripheral and central airways.

Methods or Approach:
The following tests were performed on smokers and nonsmokers: maximal expiratory flow volume curves while breathing air or a helium-oxygen mixture (79 percent He, 21 percent O_2); airway resistance and thoracic gas volume by body plethysmography; and closing volume by SF_6 bolus method. In smokers, all tests (except closing volume) were conducted before and after smoking one cigarette.

Results to Date:
Closing volume, airway resistance, V_{max}, FEV_1, and MMF could not distinguish smokers from nonsmokers; however, two groups could be distinguished by volume of isoflow, which was found to be much more sensitive than SF_6 closing volume for detecting small airways abnormalities. There were no significant changes in FEV_1, MMF, V_{max}, and thoracic gas volume after smoking one cigarette; however, there were significant increases in airway resistance (significant decrease in specific airway conductance) and volume of isoflow. Effect of smoking a cigarette was almost immediate; mean duration of effect on airway resistance was shorter than on volume of isoflow.

Future Plans:
The effect of smoking one cigarette on SF_6 closing volume and on the slope of phase III of the single-breath nitrogen washout curve is being studied.

Project Dates:
1980–1985.

Financial Support:
Fujita-Gakuen Health University, Japan.

0364. HOKKAIDO UNIVERSITY, RESEARCH INSTITUTE OF APPLIED ELECTRICITY, Laboratory for Physiology, Sapporo, Japan 060.

Project Title:
Acute Effects of Tobacco Smoke on Lung and Brain Microcirculation in Bullfrogs.

Principal Investigators:
Koyama, T.; Araiso, T.; Arai, T., et al.

Objective:
To determine the different modes of response to tobacco smoke in microcirculation.

Methods or Approach:
Receptors for vasoactive substances, which have nonuniform distribution in the microvasculature of organ tissues, were studied in bullfrogs and rabbits. The microcirculation of

exposed brain of the bullfrog was observed under a microscope connected to a videocamera and the diameter of individual vessels was measured simultaneously. Tobacco smoke was introduced via a balloon catheter inserted through the trachea into the lung.

Results to Date:
Measurements of pulmonary circulation of bullfrogs showed that blood flow velocity in the pulmonary capillary bed increased following tobacco smoke inhalation. However, calculated vascular resistance increased; ventricular blood pressure increased more than blood flow velocity.

Future Plans:
Effects of tobacco smoke on microcirculation of rabbits fed a diet containing cholesterol will be investigated.

Project Dates:
October 1984–April 1986.

Financial Support:
Research Institute of Applied Electricity, Japan.

0365. HOKKAIDO UNIVERSITY, SCHOOL OF MEDICINE, First Department of Medicine, Sapporo, Japan 060.

Project Title:
Effects of Smoking on Ventilatory Responses to Hypoxia and Hypercapnia in Man.

Principal Investigators:
Kawakami, Y.; Yamamoto, H.

Objective:
To clarify whether acute and chronic exposure to tobacco smoke influences respiratory chemosensitivity to hypoxia and hypercapnia in man.

Methods or Approach:
Ventilatory responses to hypoxia and hypercapnia were evaluated separately, while arterial blood gases were controlled with a dual control system. Chronic effects of tobacco smoke were measured on monozygotic (fraternal) twin pairs in whom genetic background is assumed to be equal. Acute effects of tobacco smoke were estimated by applying smoke to subjects while measuring ventilatory responses. To determine whether nicotine is involved in the acute effect, smoke was passed through a water bottle (nicotine is highly soluble in water).

Results to Date:
Twin pairs who smoked had significantly higher ventilatory response to hypoxia, while ventilatory response to hypercapnia was similar in smoking and nonsmoking twin pairs, indicating that peripheral (carotid) chemoreceptor is influenced by tobacco smoke (possibly nicotine). Acute exposure to tobacco smoked raised ventilatory response to hypoxia but not to hypercapnia. Smoke that had been passed through water did not have such effect. Results indicate that smoke constituents (possibly nicotine) stimulate peripheral chemoreceptors but not the central chemoreceptive area.

Project Dates:
April 1981–December 1984.

Financial Support:
Education Ministry of Japan.

Reference:
Kawakami, Y.; Yamamoto, H.; Yoshikawa, T., et al. "Respiratory Chemosensitivity in Smokers. Studies on Monozygotic Twins." *American Review of Respiratory Disease* 126(6):986-990, December 1982.

0366. HOKKAIDO UNIVERSITY, SCHOOL OF MEDICINE, First Department of Medicine, Sapporo, Japan 060.

Project Title:
Relationship Between Smoking Habits and Serum Antibody in Farmer's Lung Disease.

Principal Investigator:
Honma, Y.

Objective:
To examine relationship between time course of antibody titer and smoking habits in farmers in a northern part of Hokkaido Island.

Methods or Approach:
Between 1979 and 1984, 92 farmers were examined twice for antibody titer *Micropolyspora faeni*. Titer was analyzed with a counter immunoelectrophoresis (Hollister Stier). Smoking habit, age, sex, vocational history, and worktime in the cowshed were also determined.

Results to Date:
Positive antibodies were found in 4 of 44 farmers who smoked; 13 of 48 nonsmokers had positive antibody. Results indicate that smoking is related to serum antibody titer to *Micropolyspora faeni*.

Project Dates:
1979–1984.

Financial Support:
Hokkaido Prefecture, Japan.

0367. INSTITUTE OF ENVIRONMENTAL TOXICOLOGY, 2-772 Suzuki-cho, Kodaira-shi, Tokyo, Japan 187.

Project Title:
Effects of Antioxidants on Toxicity and Carcinogenicity of Tobacco Smoke.

Principal Investigators:
Harada, T.; Maita, K.; Tsuda, S., et al.

Objective:
To determine whether dietary intake of antioxidants can prevent biological damage elicited by cigarette smoke inhalation in hamsters.

Methods or Approach:
Male Syrian golden hamsters are exposed to cigarette smoke in a Hamburg II smoking machine and maintained on diets containing various amounts of antioxidants such as BHT, quercetin, rutin, disulfiram, glutathione, vitamin E, and vitamin C. Studies range from 3 to 24 months. Animals are sacrificed and hematological, biochemical, and pathological tests are conducted.

Results to Date:
Results suggest that vitamin C and quercetin may have some ameliorative effects on the biological damage elicited by cigarette smoke. In the vitamin C supplemented group, body weight gain and food efficiency were improved compared with smoke-exposed controls. Pulmonary macrophage mobilization and incidence of rhinitis were also inhibited. In the quercetin-supplemented group, thickening of the laryngeal mucosa was significantly inhibited. Other antioxidants did not show any beneficial effect on smoke inhalation toxicity.

Future Plans:
Further study will determine whether dietary quercetin supplement can prevent neoplastic changes induced by tobacco smoke in the larynx of hamsters.

Project Dates:
April 1981–March 1986.

Financial Support:
Japan Tobacco and Salt Public Corporation.

0368. INSTITUTE OF PUBLIC HEALTH, 4-6-1, Shirokanedai, Minato-ku, Tokyo, Japan 108.

Project Title:
Application of Tobacco Smoke Dosage Methods for Conscious Experimental Animals.

Principal Investigators:
Asano, M.; Ohkubo, C.
Objective:
To establish experimental smoking methods for rabbits and small rodents.
Methods or Approach:
A smoking mask and an electrically driven smoke dosage apparatus were manufactured for conscious rabbits, and cardiovascular and pulmonary effects of tobacco smoking were determined. Also, a tobacco smoke dosage arrangement applicable to experiments in smaller rodents was developed. The airtight plastic mask, equipped with a special pipe, was used for cardiovascular experiments in conscious rabbits. An electrically driven double-cylinder syringe for precise tobacco smoke dosage was devised. Smoke was made qualitatively and quantitatively and puffed into selected sites of the respiratory tract.
Results to Date:
Pharmacological effects of inhalation of various nicotine derivatives and application of filter tips to cigarettes were clearly demonstrated by means of the mask and the smoke dosage cylinder. Moreover, physiological and pathological effects of chronic smoking with and without use of Cambridge filters were differentiated.
Future Plans:
Investigations will be carried out on pharmacological characteristics of tobacco smoke in different sites of the respiratory tracts of rabbits with the smoke dosage apparatus. Effects of autonomic nervous blockade on nasopharyngeal reflexes due to sidestream and mainstream smoke of various types of tobacco in rabbits will be studied. The smoking method and tobacco smoke dosage will be standardized by using the mask and dosage apparatus in rabbits and small rodents.
Project Dates:
April 1972–continuing.
Financial Support:
Japan Institute of Public Health; JTSPC.

0369. INSTITUTE OF PUBLIC HEALTH, 4-6-1, Shirokanedai, Minato-ku, Tokyo, Japan 108.

Project Title:
Studies on Antidotic Substances in Pine-Oleoresin Against Cardiovascular and Microvascular Effects of Tobacco Smoking in Man and Animals.

Principal Investigators:
Asano, M.; Ohkubo, C.
Objective:
To study cardiovascular and microcirculatory responses to tobacco smoking and administration of antinicotinic substances extracted from pine oleoresin; develop practical antidotic procedures to smoking.
Methods or Approach:
Substances extracted from pine oleoresin are tested for antinicotinic action in vitro and in vivo. Measurements include electrocardiogram, blood flow, blood pressure, skin temperature, and plethysmogram, used to assess the value of a substance as an antidote in man and animals.
Results to Date:
Appropriate dosages of tobacco smoke evoke distinct cardiovascular and microvascular responses. D-pimaric and dehydroabietic acids, extracted from pine oleoresin and applied to cigarettes, appears to exert antinicotinic action when cigarettes are smoked. This extract may be a promising antidote to tobacco smoking injuries.
Future Plans:
Studies will include (1) the possibility of chronic effects of d-pimaric and dehydroabietic acids on cardiovascular and pulmonary function in rabbits; (2) the possibility of harmless application of the acids to tobacco smoking in man; and (3) pharmacological antinicotinic effects on the catecholamine release mechanism and on metabolism of nicotine.
Project Dates:
April 1960–continuing.
Financial Support:
Japan Institute of Public Health; JTSPC.

0370. INSTITUTE OF PUBLIC HEALTH, 4-6-1 Shirokanedai, Minato-ku, Tokyo, Japan 108.

Project Title:
Biochemical Studies on Various Substances Related to Nicotine.

Principal Investigators:
Ohkubo, C.; Asano, M.
Objective:
To study the biochemical and physiological effects of nicotine-related substances.
Methods or Approach:
Spectrophotometric methods are used to investigated effects of nicotine-related substances in blood, adrenal glands, liver, and other tissues and organs. Physiological effects on the cardiovascular and pulmonary system are studied in conscious rabbits by inhalation with a nebulizer. Toxicological effects are studies using *Branchiura sowerbyi*.
Results to Date:
Nicotine was most effective in pyridine derivatives on cardiovascular and pulmonary functions in rabbits. L-Nicotine was more effective than D-nicotine. Pyridine also had physiological effects.
Future Plans:
Investigation will attempt to elucidate what composition has the most characteristic structural features of nicotine and its related compounds.
Project Dates:
April 1975–continuing.
Financial Support:
Institute of Public Health, Japan.

0371. INSTITUTE OF PUBLIC HEALTH, 4-6-1, Shirokanedai, Minato-ku, Tokyo, Japan 108.

Project Title:
Physiological and Hygienic Studies on Smoking Tobacco in Man and Animals.

Principal Investigators:
Asano, M.; Ohkubo, C.
Objective:
To study cardiovascular, microvascular, pulmonary, and psychomotor responses in man and animals to smoking under varying experimental conditions including passive smoking;

establish practical preventive procedures against tobacco smoking in man.

Methods or Approach:

Measurements of hemodynamic, respiratory, and psychomotor parameters are used to assess differences between responses to varying experimental smoking conditions in man and animals. A "constant temperature" room is used to study influences of ambient temperature on responses to tobacco smoking. For rabbits, two smoke-dosage methods are applied. Acute cardiovascular and pulmonary responses to (1) active and passive smoking, (2) preprandial and postprandial smoking, and (3) smoking with and without alcohol drinking were compared under controlled conditions. Psychomotor effects and cardiovascular effect of smoking concurrent with physical exercise were also investigated.

Results to Date:

Acute cardiovascular and pulmonary responses to sham, placebo, and cigarette smoking and chewing nicotine gum in controlled dosage were evidenced in rabbits and man. In habitual smokers, seasonal variations of some responses occurred. The physiological efficacy of filter-tipped cigarettes against the acute effects of smoking was shown in man and rabbits.

Future Plans:

In man, cardiovascular and psychomotor effects of cigarette smoking concurrent with physical and/or mental exercises will be investigated. In rabbits, acute cardiovascular responses to smoking cigarettes with different types of filter tips and to inhaling carbon monoxide in various concentrations will be determined. Physiological and pathological studies on chronic smoking will also be carried out.

Project Dates:

April 1960–continuing.

Financial Support:

Institute of Public Health, Japan; JTSPC.

0372. INSTITUTE OF PUBLIC HEALTH, 4-6-1, Shirokanedai, Minato-ku, Tokyo, Japan 108.

Project Title:

Physiological and Biochemical Studies on Tobacco Smoking in Experimental Atherosclerosis.

Principal Investigators:

Asano, M.; Ohkubo, C.; Hirokawa, A., et al.

Objective:

To study physiologically and biochemically the role of tobacco smoking in experimental atherosclerosis in rabbits.

Methods or Approach:

Acute and chronic microscopic effects of tobacco smoke inhalation and a cholesterol-supplemented diet are investigated on the microvascular net within a rabbit ear chamber. Concurrently, hematological and biochemical analysis of blood and tissue is made concerning lipids, catecholamines, and corticoids. In addition, light and electron microscopy are used to analyze structural changes in atherosclerotic processes in the circulatory system.

Results to Date:

Smoke inhalation alone induced a marked, short-lasting increase in adhesiveness of leukocytes to microvascular lumen following an instantaneous vasoconstricting state, and accelerated increased adhesiveness that developed during chronic cholesterol feeding. Long-term repetition of smoke inhalation in combination with cholesterol feeding enhanced hematological changes in behavior and sludging, which were also induced by chronic cholesterol feeding alone.

Future Plans:

Investigations will attempt to clarify the separate or combined participation of nicotine and carbon monoxide in the vital microscopic changes in experimental atherosclerosis, and will test possible antiatherogenic treatments from vital microscopic and histologic points of view.

Project Dates:

April 1980–continuing.

Financial Support:

JTSPC; Institute of Public Health, Japan.

0373. JAPAN TOBACCO AND SALT PUBLIC CORPORATION, CENTRAL RESEARCH INSTITUTE, Yokohama, Japan 227.

Project Title:

Indoor Air Pollution With Tobacco Smoke.

Principal Investigators:

Ishizu, Y.; Matsuo, T.

Objective:

To measure the actual concentration of pollutants generated by tobacco smoke in real rooms; develop an effective method for maintaining a comfortable environment even when there is smoking.

Methods or Approach:

Numerical computation of a three-dimensional scheme was carried out with various positions of inlet and outlet to find an air flow pattern for the most effective ventilation. Results were compared with experimental data.

Results to Date:

It was found that the most effective ventilation is achieved when an outlet position is at a considerable distance from an inlet position.

Future Plans:

A study will be conducted on how to reduce the odor of tobacco smoke in a room.

Project Dates:

April 1980–March 1985.

Financial Support:

JTSPC.

0374. JAPAN TOBACCO AND SALT PUBLIC CORPORATION, CENTRAL RESEARCH INSTITUTE, 6-2 Unegaoka, Midori-ku, Yokohama, Kanagawa, Japan 227.

Project Title:

The Distribution of Cigarette Smoke Components Between Mainstream and Sidestream Smoke.

Principal Investigators:

Sakuma, H.; Kusama, M.; Sugawara, S.

Objective:

To determine differences between deliveries of cigarette smoke components in mainstream and sidestream smoke.

Methods or Approach:

Acidic compounds were trapped by Cambridge filter (Cf) pads and alkali trap, and bases by Cf pads and acidic trap. Middle- and higher-boiling compounds, including neutral ones, were trapped from sidestream smoke with Cf pad, Elmenhorst trap, and acetone trap. For mainstream smoke, Cf pad and acetone trap were used. Almost all components were analyzed by gas chromatography, using a FID or FTD; ammonia was analyzed photometrically with a Technicon AutoAnalyzer.

Results to Date:

Distribution ratios of 15 phenols, 14 organic acids, 35 bases, and 17 neutral compounds between sidestream (SS) and

mainstream smoke (MS) were determined for cigarettes made from bright, burley, Turkish, and domestic (matsukawa) tobacco. SS/MS ratios of bases were generally large, especially ammonia (37.4-63.6), 3-vinylpyridine (19.4-34.2), 3-cyanopyridine (10.0-17.3), pyrrole (9.0-13.7), nicotyrine (8.4-14.3), and pyridine (6.5-10.8). Ratios of relatively low boiling neutral compounds were also large: limonene (4.2-12.1), 2-furaldehyde (4.9-7.4), cyclotene (5.6-10.0), and 2,4-pentadiene-4-olide (5.2-8.9). Relatively high-boiling neutral compounds and acidic compounds generally showed relatively small SS/MS ratios.
Project Dates:
April 1981–June 1984.

0375. JAPAN TOBACCO AND SALT PUBLIC CORPORATION, KYOTO SENBAI HOSPITAL, 447 Myo-hoin-Maegawa-cho, Higashiyama-ku, Kyoto, Japan 605.

Project Title:
Effect of Smoking in Man: Changes of the Tobacco Smoke Components in Biological Fluids and Several Biochemical Variables in Relation to Tobacco Smoking.

Principal Investigators:
Muranaka, H.; Tanida, T.; Higashi, E., et al.
Objective:
To (1) determine levels of nicotine, cotinine, and hydroxyproline (HOP) in urine; (2) study changes in plasma and urine levels of nicotine, cotinine, and thiocyanate; and (3) determine changes in carboxyhemoglobin (COHb) and expired carbon monoxide (CO) and urinary HOP levels in relation to tobacco smoking habit.
Methods or Approach:
Nicotine and cotinine were determined by Hitachi FTD gas chromatograph; SCN and HOP were estimated with Technicon Autoanalyzer II. COHb and expired CO were measured with IL 282 CO-Oximeter and CO TEC (model CM 2510), respectively. Blood and urine samples were collected from nonsmokers and smokers (classified into three groups according to level of daily consumption). Urinary excretion of nicotine, cotinine, thiocyanate, and HOP were represented as the ratio to urinary creatinine.
Results to Date:
Differences in nicotine/creatinine, cotinine/creatinine, and thiocyanate/creatinine ratios and in plasma cotinine and plasma thiocyanate were statistically significant ($p=0.01$) among the four groups. However, the difference in HOP/creatinine ratio was not significant ($p=0.5$). All other parameters were also significantly correlated with daily cigarette consumption (Spearman Rank Correlation Coefficient).
Future Plans:
Urinary desmosine and hydroxyproline excretion will be determined and investigated in relation to smoking.

0376. JICHI MEDICAL SCHOOL, Division of Respiratory Diseases, Minamikawachi-machi, Kawachi-gun, Tochigi, Japan 329-04.

Project Title:
Variation of Nicotine Concentration in Daily Environment.

Principal Investigators:
Kira, S.; Arai, T.; Fukui, J., et al.
Objective:
To elucidate the mode of exposure regarding atmospheric nicotine levels as a sensitive marker of passive smoking.
Methods or Approach:
A solid state sampling method was used. Nicotine was collected by drawing air through two tubes containing 0.4 g of acid-treated diatomite (Uniport-KA in series), desorbed with alkaline methyl alcohol after adding internal standard quinoline, and concentration was determined by a gas chromatograph with a flame thermionic detector ($<0.5\ \mu g/m^3$ of nicotine can be measured by this method). Nicotine monitoring was conducted, with sampling time intervals of from 20 to 120 minutes, at several offices, hospital lobbies, party rooms, and automobiles during usual daily activities.
Results to Date:
In offices and lobbies, daytime nicotine level ranged from 4 ± 5 to $15 \pm 8\ \mu g/m^3$ (mean ± SD), while a high nicotine level of $90 \pm 44\ \mu g/m^3$ was obtained in a poorly ventilated dinner party room. In automobiles with no, modest, and moderate ventilation, nicotine concentration was 80 ± 95, 35 ± 9, and $6 \pm 3\ \mu g/m^3$, respectively, under similar smoking conditions (4 ± 3 cigarettes/hour). Data indicate that even in a particular closed space, the atmospheric nicotine exposure level can fluctuate widely from spot to spot and from time to time.
Future Plans:
Current plans are to monitor personal nicotine exposure in daily life by examining cotinine and nicotine in urine and blood and fluctuations in nicotine levels in the daily environment and to detect subtle changes in physiological parameters, if any.
Project Dates:
April 1982–continuing.
Financial Support:
JTSPC.

0377. JUNTENDO UNIVERSITY, SCHOOL OF MEDICINE, 2-1-1 Hongo, Bunkyo-ku, Tokyo, Japan 113.

Project Title:
Effect of Cigarette Smoke Exposure on Lung Metabolism.

Principal Investigators:
Homma, H.; Kitamura, S.; Chijimatsu, Y.
Objective:
To study effects of nicotine and cigarette smoke on blood and histamine, serotonin, ACE activity, 6-keto $PGF_1\alpha$, and thromboxane B_2 in animal and human materials.
Methods or Approach:
Studies were conducted with 12 mongrel dogs, 70 guinea pigs, and 12 healthy human volunteers. Nicotine was injected in the dogs; quinea pigs were placed in a box and cigarette smoke was introduced. In healthy volunteers, five cigarettes for men and three cigarettes for women were smoked within 5 to 7 minutes.
Results to Date:
In the dogs, injection of 10 and 50 $\mu g/kg$ nicotine increased serum histamine level and decreased serum serotonin level. In guinea pigs, smoke exposure increased plasma histamine and serotonin levels, while serum ACE level remained unchanged. Cigarette smoking by human volunteers caused increases in serum 6-keto $PGF_1\alpha$ and thromboxane B_2.
Future Plans:
The effect of smoking on serum levels of leukotrienes will be investigated.
Project Dates:
April 1984–March 1986.
Financial Support:
JTSPC.

0378. JUNTENDO UNIVERSITY, SCHOOL OF MEDICINE, 2-1-1 Hongo, Bunkyo-ku, Tokyo, Japan 113.

Project Title:
Effect of Cigarette Smoking on Protective Mechanisms in Human Body.

Principal Investigators:
Homma, H.; Kira, S.; Inatomi, K., et al.
Objective:
To study effects of cigarette smoking on bronchoalveolar lavage fluid (BALF) and complements in the blood.
Methods or Approach:
BALF studies were conducted on 91 cases with various respiratory diseases including sarcoidosis and interstitial pneumonia, divided into smokers and nonsmokers. BAL was repeated three times and cells, total protein (TP), and carcinoembryonic antigen (CEA) in fluid were studied. For complement levels, 21 healthy persons (14 smokers, 6 ex-smokers, and 1 nonsmoker) were studied. Components of complement in the blood were measured before smoking one cigarette, and 10 minutes, 1 hour, and 24 hours after smoking.
Results to Date:
In sarcoidosis and interstitial pneumonia, there were no differences in total number of cells, lymphocytes, and neutrophils between smokers and nonsmokers. CEA/TP ratio (ng/mg) was often elevated in smokers with interstitial pneumonia, especially when complicated with lung cancer. Cigarette smoking caused no changes in CH50 , but ACH50 was decreased. Blood ACH50 and C_3c were significantly low in smokers. Results suggest that an alternative pathway was activated in smokers.
Project Dates:
April 1983–March 1985.
Financial Support:
JTSPC.

0379. KOBE UNIVERSITY, SCHOOL OF MEDICINE, Department of Obstetrics and Gynecology, 5-1 Kusunoki-cho 7-Chome, Chuo-ku, Kobe, Japan 658.

Project Title:
Mechanism of Fetal Growth Retardation Caused by Smoking During Pregnancy.

Principal Investigators:
Mochizuki, M.; Maruo, T.; Masuko, K., et al.
Objective:
To clarify the mechanism of retarded fetal growth in pregnant women who smoke.
Methods or Approach:
Clinical studies were conducted with 124 pregnant women (at least 28 weeks gestational age). Factors analyzed were fetoplacental function (human placental lactogen (hPL), E_3), utero-placental circulation (dehydroepiandrosterone sulfate (DHA-S) loading test and NST during smoking), histopathological findings of chorionic villi, and cotinine levels in maternal blood, maternal urine, and umbilical cord blood.
Results to Date:
In heavy smokers, urinary estriol and serum levels of hPL were lower than in nonsmokers. There was no difference in maternal nutrition between smokers and nonsmokers. Heavy smokers demonstrated lower conversion of DHA-S to estradiol than nonsmokers and cotinine levels in maternal blood and umbilical cord blood of heavy smokers were higher than in nonsmokers. Microscopic examination showed atrophic and hypovascular changes in placental villi from mothers who smoked. Results suggest that retarded fetal growth in heavy smokers is due to impairment of uteroplacental circulation as a result of the vasoconstricting effect of nicotine.
Future Plans:
Studies will be carried out with pregnant rats to elucidate effects of nicotine on carbohydrate lipid metabolism in the feto-maternal system.
Project Dates:
April 1980–March 1988.
Financial Support:
JTSPC.

0380. KYOTO UNIVERSITY, SCHOOL OF MEDICINE, Division of Clinical Nutrition, 54 Kawara-cho, Shogoin, Sakyo-ku, Kyoto Japan 606.

Project Title:
Effects of Active and Passive Smoking on Urinary Cotinine Excretion in Smokers and Nonsmokers.

Principal Investigator:
Matsukura, S.
Objective:
To investigate effects of smoking on urinary cotinine excretion in smokers and nonsmokers; obtain quantitative information on passive smoking in the general environment.
Methods or Approach:
Urine samples were collected from nonsmokers and smokers, and urinary cotinine was measured by radioimmunoassay. In nonsmokers, urinary cotinine was analyzed according to data on tobacco smoke exposure in the home, the workplace, and public places. In smokers, values were evaluated by smoking habits and cardiovascular functions.
Results to Date:
It was found that (1) urinary cotinine increases with increasing daily cigarette consumption, and (2) passive smoking occurs in the home, the workplace, and the community.
Future Plans:
The amount of smoke inhaled by nonsmokers will be estimated; urinary cotinine excretion will be determined in infants and nonsmokers at a particular company; and the effects of smoking on cardiovascular functions will be measured.
Project Dates:
April 1981–continuing.
Financial Support:
JTSPC; Ministry of Education, Culture and Science, Japan.

0381. MEDICAL COLLEGE OF OITA, Department of Public Health and Hygiene, Hazama-cho, Oita, Japan 879-56.

Project Title:
Smoker's Melanosis.

Principal Investigator:
Araki, S.
Objective:
To determine cause of melanin pigmentation in attached gingiva of lead workers; determine in smokers dose–response relationship and relation to oral cancer, reversibility (recovery after cessation of smoking), and latent period for development.
Results to Date:
Pigmentation rate was significantly higher in smokers who inhaled > 10 cigarettes/day than in nonsmokers, and tended to increase with increased tobacco consumption. Lead absorption did not appear to cause melanin pigmentation.
Future Plans:
Reversibility, latent period for onset, and relationship of gingival pigmentation to cancer will be studied.

Project Dates:
1983–1986.
Financial Support:
Medical College of Oita; Japan Ministry of Education, Science and Culture.

0382. MEDICAL COLLEGE OF OITA, Department of Public Health and Hygiene, Hazama-cho, Oita, Japan 879-56.

Project Title:
Effect of Smoking on Peptic Ulcer in Japanese Factory Workers.

Principal Investigator:
Araki, S.
Objective:
To determine incidence and prevalence rates of active and inactive peptic ulcer in Japanese factory workers; determine effect of smoking on rates.
Methods or Approach:
Sex- and age-specific rates of peptic ulcer are calculated in workers at a plastics processing factory. Effects of smoking and other major risk factors are analyzed in a case–control study.
Results to Date:
Prevalence of active and inactive peptic ulcer was 23 percent in male workers aged 31 to 60. Incidence during 1 year was ≥ 5 percent. Findings from the case–control study suggest that smoking and family history are major etiological factors. Incidence and prevalence of peptic ulcer in male factory workers in Japan appeared to be higher than elsewhere.
Future Plans:
The difference in effects of smoking on gastric and duodenal ulcers will be studied.
Project Dates:
1983–1985.
Financial Support:
Medical College of Oita; Japan Ministry of Labor.

0383. MITSUBISHI ACETATE COMPANY LTD., Tow-Filter Development Center, 3, Kaigandori, Toyama City, Japan 931.

Project Title:
Development of New Cigarette Filter.

Principal Investigator:
Sakai, T.
Objective:
To develop a new cigarette filter and study construction materials.
Methods or Approach:
Filtration, ventilation, and filter additives were studied and a new cigarette filter was developed.
Results to Date:
The pressure drop related to the new filter was demonstrated at the seventh International Tobacco Scientific Congress in Manila; the actual filter was presented at the eighth International Congress in Vienna. Patent applications have been filed; several have been approved.
Future Plans:
A new cigarette filter, with rich taste but low tar levels, using a special ventilation technique, will be developed.
Project Dates:
February 1977-1987.
Financial Support:
Mitsubishi Acetate Company Ltd.

0384. NAGOYA UNIVERSITY SCHOOL OF MEDICINE, Departments of Surgery and Preventive Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya, Aichi-ken, Japan 466.

Project Title:
Effects of Smoking on Disease Progression of Buerger's Disease.

Principal Investigators:
Shionoya, S.; Matsubara, J.; Sasaki, R., et al.
Objective:
To determine whether smoking is related to progression of Buerger's disease.
Methods or Approach:
An epidemiologic case–control study of smoking habits was conducted among patients with Buerger's disease. Followup of patients evaluated clinical course of the disease, with special reference to smoking.
Results to Date:
Almost all patients (97.8 percent) were smokers, and Brinkman index was significantly higher in patients than in controls. In 50 percent of patients who continued to smoke, ischemic symptoms were exacerbated, but symptoms worsened in only 8 percent of patients who quit smoking.
Future Plans:
Plans include (1) experimental study on effects of smoking on function of vascular endothelium; (2) measurement of MAO activity in platelets and carboxyhemoglobin in blood of patients with Buerger's disease; and (3) effects of smoking on cellular sensitivity to collagen in patients with Buerger's disease.
Project Dates:
April 1984–March 1987.
Financial Support:
Ministry of Health and Welfare of Japan.

0385. NATIONAL CANCER CENTER RESEARCH INSTITUTE, Biophysics Division, Tsukiji 5-1-1, Chuo-ku, Tokyo, Japan 104.

Project Title:
Generation of Active Oxygens From Cigarette Smoke and Resultant Strand Breaks of DNA in Cultured Human Cells.

Principal Investigators:
Nakayama, T.; Kaneko, M.; Kodama, M., et al.
Objective:
To determine whether cigarette smoke, a tumor promoter that stimulates alveolar macrophages to generate O_2 or H_2O_2, will also directly generate active oxygens via redox reactions of organic free radicals.
Methods or Approach:
Cigarette smoke was trapped by passing through a buffered solution or dimethylsulfoxide solution. H_2O_2 and O_2 were detected by ABTS/peroxidase method and NBT method, respectively. Strand breaks of DNA were estimated by alkaline elution technique.
Results to Date:
Amount of active oxygens in smoke solutions increased with time of autoxidation at room temperature. Level of H_2O_2 detected was 4 μg/cigarette. Human lung carcinoma cells, incubated at 20° with cigarette smoke solutions, exhibited DNA strand breaks that could be inhibited by catalase, superoxide dismutase, benzoate, or DETAPAC, indicating involvement of hydroxide ion by Haber-Weiss reaction of the Fenton type.

Future Plans:
Effect of superoxide dismutase and catalase on sister chromatid exchange or chromosome aberration by cigarette smoke solutions will be investigated.
Project Dates:
April 1985–October 1985.
Financial Support:
National Cancer Center Research Institute, Japan.

0386. NATIONAL INSTITUTE OF HYGIENIC SCIENCES, Division of Mutagenesis, 1-18-1 Kamiyoga, Setagaya-ku, Tokyo, Japan 158.

Project Title:
Cytogenetic Effects of Gaseous and Volatile Chemicals on Mammalian Cells In Vivo.

Principal Investigators:
Sofuni, T.; Hayashi, M.; Sawada, M., et al.
Objective:
To examine gaseous and volatile chemicals for potential to induce chromosome aberrations in mice in vivo.
Methods or Approach:
The micronucleus test was carried out on 8-week-old ddY mice exposed to the gaseous phase of a test chemical for 3 hours. Femoral marrow cells were collected 24 hours after initiation of exposure, and micronucleated polychromatic erythrocytes (MNPCE) were examined in 1,000 polychromatic erythrocytes in each animal. Carcinogens such as benzo(*a*)pyrene and related compounds, which have already been examined in cultured Chinese hamster cells, will be included in the test series.
Results to Date:
Ethylene oxide, positive in the in vitro test, was also positive in the in vivo test; frequency of MNPCE indicated a significant concentration-dependent increase. However, methyl acrylate, also positive in the in vitro test, was negative in the in vivo test, without any significant increase of MNPCE frequencies. Benzene (negative in the in vitro test) was positive in the in vivo test.
Future Plans:
A variety of chemicals (especially air pollutants) will be examined. Improvements in protocol, including extension of exposure time, will be made.
Project Dates:
April 1982–March 1984.
Financial Support:
Environmental Agency, Japan.

0387. NATIONAL INSTITUTE OF PUBLIC HEALTH, 4-6-1, Shirokanedai, Minato-ku, Tokyo, Japan 108.

Project Title:
Physico-Chemical Studies on the Control of Indoor Air Quality.

Principal Investigator:
Matsushita, H.
Objective:
To develop analytical methods for evaluation of indoor air quality; develop methods for elimination of pollutants in indoor environment.
Methods or Approach:
Specifically, a low noise air sampler will be developed for collecting particulates in indoor air. Analytical methods will be developed for analysis of various kinds of pollutants in the indoor environment, especially carcinogens such as N-nitrosodimethylamine, nitroarenes, and polynuclear aromatic hydrocarbons. Methods will be used to evaluate indoor air quality. Several methods for eliminating indoor air pollutants will be developed and tested.
Results to Date:
A short-term method for analyzing N-nitrosodimethylamine in cigarette smoke and the indoor environment was developed. Use of the method revealed that sidestream smoke from cigarettes was one of the most important sources of nitrosamines in indoor air pollution.
Future Plans:
Studies will evaluate effect of smoking on indoor air pollution and an effective method for eliminating indoor air pollutants will be developed.
Project Dates:
April 1984–March 1987.
Financial Support:
JTSPC.

0388. SAGA MEDICAL SCHOOL, Department of Community Health Science, Saga, Japan 840-01.

Project Title:
Cancer and Other Causes of Death Among Psychiatric Patients.

Principal Investigators:
Tokudome, S.; Kono, S.; Ikeda, M., et al.
Objective:
To examine the mortality of psychiatric patients with special reference to malignant neoplasms; evaluate possible effects of smoking on cancer mortality among the patients.
Methods or Approach:
Approximately 8,000 medical records of about 3,000 Japanese psychiatric patients admitted to a sanatorium from 1945 to 1982 were reviewed. Information on name, address, sex, date of birth, date of admission, date of discharge, psychiatric diagnosis, and date of death was obtained. Patients were classified by their psychiatric diagnoses. The observed number of deaths is compared with the expected number of deaths derived from the general population. Smoking and drinking habits were also obtained from the records to evaluate possible effects on cancer mortality among the patients.
Results to Date:
Project is continuing.
Project Dates:
April 1982–1985.
Financial Support:
Ministry of Education, Japan.

0389. TOHOKU UNIVERSITY SCHOOL OF MEDICINE, Department of Internal Medicine, 1-1 Seiryomachi, Dendai, Japan 980.

Project Title:
Effect of Nicotine on the Ventilatory Response to Hypercapnia in Dogs.

Principal Investigators:
Takishima, T.; Nakamura, M.; Sasaki, M., et al.
Objective:
To study the effect of intravenous injection of nicotine on the ventilatory response to hypercapnia in anesthetized dogs.
Methods or Approach:
Dogs were anesthetized with α-chloralose and urethane; anesthesia was maintained with continuous administration. Carbon dioxide response curves for occluded tracheal pressure at 200 msec after onset on inspiration ($P_{0.2}$) and minute ventilation (V_E) versus end-tidal carbon dioxide tension

($P_{ET}CO_2$) were obtained by the rebreathing of the gas mixture containing 7 percent CO_2 and 93 percent O_2. Time courses of $P_{0.2}$ and V_E were measured before and after injection of nicotine at concentrations of 1, 4, 16, 64, and 256 µg/kg in five different groups with five dogs each.

Results to Date:
Nicotine produces biphasic ventilatory response to hypercapnia, first stimulating the respiratory center and subsequently inhibiting it, which suggests that smoking inhibits ventilatory response to hypercapnia.

Future Plans:
The effect of cigarette smoke on mucociliary transport and relaxation of magnetic iron oxide particles, placed on mucosal surface of trachea and small airways and in alveoli in dogs, will be investigated.

Project Dates:
April 1984–March 1986.

Financial Support:
Japan Monopoly Tobacco Corporation.

0390. UNIVERSITY OF OCCUPATIONAL AND ENVIRONMENTAL HEALTH, Department of Clinical Epidemiology, Yahatanishi-ku, Kitakyushu, Japan 807.

Project Title:
Drinking, Smoking and Causes of Death in Japanese Physicians.

Principal Investigators:
Kono, S.; Ikeda, M.; Tokudome, S., et al.

Objective:
To evaluate effect of drinking and smoking on various causes of death, particularly cancer and coronary disease; study interactions between smoking and drinking.

Methods or Approach:
This second followup study of male Japanese physicians, first surveyed in 1965, will survey smoking and drinking habits and extend the original followup period (1977) to 1983. The cohort consists of 5,477 men in nine prefectures in Japan.

Results to Date:
Data on smoking from the first followup are compatible with current knowledge, but the increased risk of lung cancer in the Japanese population appears to be less than in Caucasians.

Project Dates:
September 1984–December 1985.

Financial Support:
University of Occupational and Environmental Health; Fukuoka-ken Anti-cancer Society.

Reference:
Kono, S. "Drinking and Causes of Death in Japanese Physicians." *International Journal of Epidemiology* 12:437-441, 1983.

0391. YOKOHAMA CITY UNIVERSITY, SCHOOL OF MEDICINE, First Department of Internal Medicine, 3-46 Urafune-cho, Minami-ku, Yokohama, Japan 232.

Project Title:
Acute Effect of Smoking on Bronchial Responsiveness.

Principal Investigators:
Okubo, T.; Suzuki, S.; Sano, F.

Objective:
To study the acute effects of smoking on bronchial responsiveness.

Methods or Approach:
In normal subjects, bronchial responsiveness to methacholine was measured before and after smoking two cigarettes and responsiveness was compared.

Results to Date:
Neither smokers nor nonsmokers showed any changes in bronchial responsiveness after smoking cigarettes.

Future Plans:
Acute effects of smoking on bronchial responsiveness will be studied in patients with bronchial asthma and chronic obstructive lung disease.

Project Dates:
October 1984–October 1986.

Financial Support:
Yokohama City University.

MALAYSIA

0392. NATIONAL UNIVERSITY OF SINGAPORE, KANGANG KERBAU HOSPITAL FOR WOMEN, Singapore 0821, Malaysia.

Project Title:
Effects of Cigarette Smoke on Steroidogenic Enzymes of the Feto-Maternal-Placental Unit.

Principal Investigators:
Gunasegaram, R.; Longanath, A.; Peh, K.L., et al.

Objective:
To examine the effects of the constituents of cigarette smoke on functional capacity of steroidogenic enzymes concerned with synthesis of progesterone and estrogens by the feto-maternal-placental unit.

Methods or Approach:
Effect of cigarette smoke extract at varying doses on cholesterol C-20,22-desmolase ability to cleave 26-^{14}C cholesterol to ^{14}C-isocaproic acid by human corpora lutea and placentae were studied. Methods included in vitro incubation, reverse isotope dilution technique, derivatization, and establishment of radiochemical homogeneity.

Results to Date:
With the corpora lutea of pregnancy (4 to 9 weeks gestation) the maximum inhibitory effect of cigarette smoke extract on desmolase efficiency was reached at four cigarettes. In response to concentrations of the extract at one-half, one, two, and four cigarette equivalents on preparations of placentae (18 to 20 weeks gestation), a dose-dependent pattern of inhibitory effect was observed. Results imply a reduced pregnenolone supply.

Future Plans:
In vitro effects of nicotine and lobeline on steroidogenic steps between pregnenolone and estrogens will be studied.

Project Dates:
January 1982–January 1987.

Financial Support:
National University of Singapore.

Reference:
Gunasegram, R.; Phe, K.L.; Loganath, A., et al. "Inhibition of Second Trimester Human Placental Cholesterol C-20,22-Des-

molase Activity by Soluble Constituents of Cigarette Smoke." *IRCS Medical Science: Biochemistry* 10(4):322-323, 1982.

NEPAL

0393. MRIGENDRA MEDICAL TRUST, P.O. Box 2587, Kathmandu, Nepal.

Project Title:
Epidemiological Study of Tobacco Smoking Habit of Both Children and Adults in a Rural Community of Nepal With Special Emphasis on Behavioral and Attitudinal Aspects.

Principal Investigator:
Pandey, M.R.

Objective:
To (1) determine the smoking habits of youths (8 to 14 years of age) and adults (>20 years of age) of both sexes; (2) test the WHO standardized questionnaire in the context of the national situation; (3) determine usefulness of the tool; (3) provide data on attitudes and beliefs of people; and (4) suggest smoking control measures that might be effective with the population.

Methods or Approach:
A cross-sectional survey was conducted in a rural community of the hill region of Nepal, using the WHO standarized smoking survey questionnaire with slight modifications to suit local conditions. The questionnaire was pretested in a nearby village. Door-to-door visits were made and information recorded by a trained interviewer. Data were analyzed manually and by computer. Attitudes, beliefs, and aspects of behavior were observed in relation to relevant sociodemographic variables. The survey was conducted between December 1983 and February 1984.

Results to Date:
For adults, the modified questionnaire was satisfactory and useful as a tool for collecting information on smoking. Overall prevalence of smoking was 73.7 percent; 85.4 percent of men and 62.4 percent of women were smokers, an increase of 4.9 percent over 1980. The less educated and otherwise socially deprived people are more vulnerable to the hazards of smoking. Although the majority of adult smokers, both male and female, are aware of the hazards of smoking, they are not concerned about the harmful effects on themselves or on nearby nonsmokers. There is an urgent need to plan and implement appropriate smoking control measures in Nepal. Data analysis of the youth survey is under way.

Project Dates:
December 1983–March 1985.

Financial Support:
WHO.

NETHERLANDS

0394. AGRICULTURAL UNIVERSITY, Department of Toxicology, De Dreijen 12, 6703 BC Wageningen, The Netherlands.

Project Title:
Genotoxicity of Cigarette Smoke Condensate in Mammalian Cells and Antimutagenic Activity of Some Naturally Occurring Compounds Towards Cigarette Smoke Condensate and Benzo(*a*)pyrene in *Salmonella typhimurium*.

Principal Investigators:
Jongen, W.M.F.; Van der Hoeven, J.C.M.

Objective:
To investigate the initiating and promoting capacities of cigarette smoke condensate (CSC); test for antimutagenic activity toward CSC and benzo(*a*)pyrene (BaP).

Methods or Approach:
Initiating and promoting capacities of CSC were studied in different assays using mammalian cells. Mutagenicity of CSC was investigated in a co-cultivation system using primary chick embryo hepatocytes and V79 Chinese hamster cells. Several compounds occurring in food were tested for antimutagenic activity toward CSC and BaP. Antimutagenicity was determined in the salmonella/mammalian microsome assay using strain TA98 in the presence of Aroclor 1254 induced rat liver homogenate.

Results to Date:
CSC was negative in SCE assay both with and without metabolic activation. In the HGPRT assay, no direct mutagenicity was observed. After metabolic activation, a considerable increase in the number of mutants was found. Comparison of different metabolizing systems showed that noninduced chick hepatocytes, liver homogenate of noninduced chick embryos, and liver homogenate of rats pretreated with Aroclor 1254 generated comparable numbers of mutants. Inhibition of metabolic cooperation is thought to be associated with tumor-promoting ability of compounds. CSC appeared to inhibit metabolic cooperation between a mixed culture of V79 cells. A dose-related increase in inhibition of metabolic cooperation was observed at nontoxic doses. Ellagic acid riboflavin, chlorophyllin, chlorophyll a, and chlorophyll b caused a dose-related reduction of CSC and BaP mutagenicity. Ascorbic acid, β-carotene, tocopherol-acetate, chlorogenic acid, and butylhydroxy anisole did not influence mutagenicity of CSC and BaP. The similarity in results for CSC and BaP indicates a comparable mechanism of inhibition by compounds investigated.

0395. INSTITUTE CIVO-TOXICOLOGY AND NUTRITION TNO, Department of Biological Toxicology, P.O. Box 360, 3700 AJ, Zeist, The Netherlands.

Project Title:
Co-Mutagenic Activity of Cigarette Smoke Condensate and Norharman in *Salmonella typhimurium* and Chinese Hamster Ovary Cells.

Principal Investigators:
Wilmer, J.W.G.M.; Rutten, A.A.J.J.L.

Objective:
To investigate the co-mutagenic activity of cigarette smoke condensate (CSC) and norharman (NH).
Methods or Approach:
The Ames test was used with a number of cigarette smoke constituents and a variety of known mutagens/carcinogens (alkylating agents, aromatic amines, polycyclic hydrocarbons). A comparative investigation was carried out with the known co-mutagenic compound NH, which occurs in cigarette smoke in amounts from 4 to 20 μg/cigarette. Co-mutagenic activity of CSC and NH was investigated in a mammalian cell culture system using induction of sister chromatid exchanges as the genotoxic parameter.
Results to Date:
Results did not indicate a synergistic effect between CSC and direct-acting mutagens in the Ames test. Strong synergistic effects were found between CSC and a number of aromatic amines, compounds that need metabolic activation to be mutagenic. Blocking of enzymatic detoxification pathways by CSC may result in an increased amount of ultimate mutagenic metabolites formed by metabolic activation of aromatic amines. The direct mutagens mitomycin C and N-methyl-N-nitro-N-nitrosoguanidine, tested in combination with CSC and NH, did not show any co-mutagenic activity; however, the indirect mutagens 2-acetylaminofluorene, 2-aminofluorene, N-hydroxy-acetylaminofluorene, 2-aminoanthracene, cyclophosphamide, and benzo(*a*)pyrene showed (in combination with CSC and NH) a co-mutagenic effect at two dose levels. The effect was dependent on the concentration of S-9 in the medium.
Future Plans:
Experiments with isolated hepatocytes are in progress to elucidate the importance of metabolic activation and deactivation pathways for the synergism observed between CSC and indirect-acting mutagens.

0396. INSTITUTE CIVO-TOXICOLOGY AND NUTRITION, P.O. Box 360, 3700 AJ, Zeist, The Netherlands.

Project Title:
Nutrition and Experimentally Induced Lung Cancer in Hamsters.

Principal Investigator:
Beems, R.B.
Objective:
To investigate the modifying effect of nutritional factors on chemically induced tumors of the respiratory tract in hamsters.
Methods or Approach:
Groups of 40 Syrian golden hamsters of each sex were fed diets containing various levels of vitamin A, β-carotene, or selenium, or diets containing a high level of saturated or unsaturated fat. After a 1- to 5-month adaptation period, respiratory tract tumors were induced by intratracheal instillation of benzo(*a*)pyrene attached to ferric oxide. Tumor response was used as an indicator for the modifying effect of dietary factors.
Results to Date:
Unsaturated fat was more effective than saturated fat in enhancing tumor response in the respiratory tract. Tumors in other organs were also enhanced by dietary fat. Vitamin A did not reduce tumor response in the respiratory tract; however, preneoplastic changes showed a distinct and statistically significant inverse association with oral vitamin A dose. Dietary selenium and β-carotene did not influence incidence of respiratory tract tumors or the incidence of preneoplastic lesions.
Future Plans:
The relationship between dietary vitamin A or β-carotene intake and serum levels will be investigated.
Project Dates:
January 1980–December 1984.
Financial Support:
Netherlands Cancer Foundation.

0397. MUNICIPAL HEALTH DEPARTMENT, Schiedamsedijk 95, 3011 Rotterdam, The Netherlands.

Project Title:
Kaunas-Rotterdam Intervention Study (KRIS).

Principal Investigators:
Sturmans, F.; Schuurman, J.H.
Objective:
To (1) study the recruitment of a population into two cardiovascular disease intervention programs; (2) examine factors affecting the subject's compliance to a given treatment regimen; (3) examine the interaction between the local medical community, the research team, and the target population; (4) study the cost-effectiveness of the intervention program; (5) compare the effectiveness of intensive treatment by the research team with treatment carried out by routine medical services; and (6) examine the feasibility of conducting a double-blind intervention trial in a population.
Methods or Approach:
The study was carried out with standardized procedures at two sites with contrasting health systems, Kaunas (Lithuania, U.S.S.R.) and Rotterdam (Netherlands). Kaunas has a State-run centralized health service providing free health care, whereas the Rotterdam health services consist mainly of private practitioners with health care costs covered by private health insurance schemes. The target population was defined as males aged 45-59 years who had their permanent residence within the selected geographical region at the start of the screening period. A sample of 4,000 was envisaged at each site. After the target population was identified, a prescreening baseline survey was conducted, partly through interviews and partly through mailed self-administered questionnaires. The baseline survey was designed to collect information from the target population regarding social and demographic characteristics, medical utilization experience, and personal attitudes toward health. The subjects in the study were then invited to participate in a screening examination consisting of the collection of medical history and some behavioral data, anthropometric measurements, ECG and blood pressure measurement, and cholesterol and glucose tolerance determination. After the screening examination, the screened population was divided into three groups–normal, borderline, and pathological. The final borderline group with stable risk factor levels and no rejection factors was recruited for a double-blind drug treatment trial. The treated and control groups were examined periodically to detect any differences in their risk factor levels and other characteristics. The pathological group was divided into two sections. One group were referred to their general practitioners or district internists for appropriate treatment while the other group were treated by the study team. Both groups were compared in terms of various end points of interest. A 10 percent sample of the normal group was reexamined at the end of the trial stage to detect the influence of screening on risk factor levels and other end points of interest. Antismoking advice was given individually to all those smoking >10 cigarettes/day. This advice was repeated at each regular checkup during a period of 5 years. In addition to the followup of the cohort of adult males, a sample of the general

practitioners in Rotterdam and district internists in Kaunas was studied. Before the start of the study, a questionnaire was administered to elicit their attitudes toward public health intervention programs. At the end of the study, the questionnaire was readministered to detect any changes in their attitudes and perceptions regarding changes in the utilization patterns of patients. Ten years after the start of the study (1982), a self-administered questionnaire was sent to all participants in the screening examination in Rotterdam to collect information regarding mortality and morbidity status and changes in smoking behavior.

Results to Date:
Results of the first year of the trial stage have been published.

Project Dates:
September 1972–1986.

Financial Support:
Dutch Municipal Health Department; Dutch Foundation for Preventive Research; Ministry of Health and Environmental Hygiene, Netherlands; Dutch Heart Foundation.

Reference:
Glasunov, I.S.; Dowd, J.E.; Baubiniene, A., et al. (Editors). *The Kaunas Rotterdam Intervention Study. Behavioral and Operational Components on Health Intervention Programmes.* New York, Elsevier/North-Holland Biomedical Press, 1981, 320 pp.

0398. STATE UNIVERSITY OF LIMBURG, Department of Health Education, P.O. Box 616, 6200 MD, Maastricht, Limburg, The Netherlands.

Project Title:
Prevention of Smoking Behaviour in Children.

Principal Investigators:
Kok, G.J.; De Vries, H.

Objective:
To analyze motives and factors that predict initiation of smoking behavior in children; develop and implement an antismoking campaign.

Methods or Approach:
By applying the Fishbein and Ajzen model, the structure of attitudinal and normative components of initiation of smoking in children aged 10 to 15 years will be analyzed. In the following 3 years, an antismoking campaign will be developed and implemented in educational settings. Special attention will be paid to the role of peer group pressure. The prevention program will be tested in a longitudinal field study of schoolchildren, utilizing an experimental research design.

Results to Date:
Project is in a preliminary phase.

Project Dates:
September 1984–September 1988.

Financial Support:
Dutch Cancer Foundation.

0399. UNIVERSITY OF AMSTERDAM, ACADEMISCH MEDISCH CENTRUM, Department of Cardiology, Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands.

Project Title:
The Long-Term Effect on Prognosis and Risk Factors of a Rehabilitation Program After a First Myocardial Infarction in Men Aged 40-55 Years.

Principal Investigators:
Vermeulen, A.; Lie, K.I.; Durrer, D., et al.

Objective:
To (1) determine if a short-term rehabilitation program can change the prognosis of middle-aged men following first myocardial infarction (MI); (2) determine which factors are involved in prognosis; and (3) determine which changes in risk factors are related to change in prognosis.

Methods or Approach:
The study cohort consisted of 98 men recruited between 1971 and 1975 from patients admitted to the coronary care unit of the department of cardiology. Each met the following conditions: (1) 40 to 55 years of age; (2) first MI; (3) admission within 6 hours after onset of complaints; (4) having no other disabling disease; (5) living in the area; and (6) cooperative. Of these, 47 were randomly assigned to an outpatient cardiac rehabilitation program. All other medical treatment and diet prescriptions were the same in both groups. Six weeks after MI, the intensive cardiac rehabilitation program (6 weeks), which included physical training, psychosocial counseling, and vocational counseling, was started.

Results to Date:
At 5-year followup, there was a significant change in progression of coronary artery disease in the group participating in the rehabilitation program (10 of 47 vs. 24 of 51, $p<0.05$). Only four men in the total cohort had not changed smoking habits; all others had either stopped smoking (40) or reduced nicotine intake (39). Smoking cessation was related to smoking habits before MI. Rehabilitation had no effect on change in smoking habits. The only difference in risk factors was lower serum cholesterol level in rehabilitated patients.

Future Plans:
Followup will be extended for another 5 years to determine whether changes are maintained.

Project Dates:
February 1971–December 1985.

Financial Support:
Preventie Fonds.

0400. UNIVERSITY OF LEIDEN, Wassenaarseweg 72, 2333 AL, Leiden, The Netherlands.

Project Title:
The Use of Tobacco as a Hallucinogenic Drug in Pre-Columbian Mexico and Europe.

Principal Investigator:
Elferink, J.G.R.

Objective:
To establish the role of tobacco as a hallucinogenic and narcotic agent in the pre-Columbian Aztec culture and in Mexico and Europe shortly after the conquest.

Methods or Approach:
Data are collected from writings of Spanish and indigenous writers of the 16th century and from European works written at about the same time. Literature is searched for information with regard to use of tobacco for medicinal, hallucinogenic, and narcotic purposes.

Results to Date:
Many writers reported that the Aztecs and the tribes of the Caribbean Islands used tobacco, either by smoking or in other ways, for its hallucinogenic and narcotic properties. In the Aztec culture, it was used mainly by those in the priesthood, to establish contact with supernatural forces.

Project Dates:
1981–1986.

0401. UNIVERSITY OF LIMBURG, P.O. Box 616, 6200 MD, Maastricht, The Netherlands.

Project Title:
Health Conceptions, Health Behaviors, and Professional Performance of School Teachers, Community Nurses, and General Practitioners.

Principal Investigators:
Adriaanse, H.; De Witte, L.; Drop, M.J.
Objective:
To determine the relationship between health conceptions, health behavior, and professional performance of health workers and educators, focusing on health educational aspects of these professions.
Methods or Approach:
Nationwide surveys were conducted in 1981 and 1983 of the following groups: (1) general population (1,278 and 1,184 persons, respectively); (2) school teachers (299 and 101); (3) community nurses (84 and 100); and (4) general practitioners (74 and 100).
Results to Date:
Results have been published.
Future Plans:
A third survey is planned for 1987.
Project Dates:
May 1981–December 1985.
Financial Support:
Foundation of the Sick, the Netherlands.
Reference:
Rijintjes, A.G.; Dubois, V.E.; Adriaanse, H.P. "Health Beliefs, Health-Related Behaviour and Professional Performance of General Practitioners: Their Role in Health Education." Proceedings of the 10th WONCA World Conference on Family Medicine, Singapore, May 20-24, 1983, pp. 203-208.

0402. UNIVERSITY OF NIJMEGEN, Department of Toxicology, Geert Grooteplein Noord 21, 6525 EZ, Nijmegen, The Netherlands.

Project Title:
Detection Methods of Industrial Carcinogens.

Principal Investigators:
Henderson, P.T.; Bos, R.P.; Jongeneelen, F.J., et al.
Objective:
To develop and evaluate methods for biological monitoring of exposure to electrophilic compounds, especially carcinogens.
Methods or Approach:
Nonselective methods for biological monitoring included urinary mutagenicity assay and thioether assay. Selective methods for determination of compounds or metabolites included gas chromatography and high performance liquid chromatography.
Results to Date:
Mutagens were found in urine of smokers, passive smokers, and nurses working with cytostatic drugs; a synergistic effect was noted in smokers. Thioether products were found in urine of smokers; traces of chemical wastes in workers exposed to methyl chloride; and carbon disulfide metabolites of polycyclic aromatic hydrocarbons in creosote workers.
Project Dates:
1977–1999.
Financial Support:
Dutch Ministry of Social Affairs.

NEW ZEALAND

0403. CANCER SOCIETY OF NEW ZEALAND, INC., Box 10340, Wellington, New Zealand.

Project Title:
Public Attitudes Towards Restraints on Smoking and Cigarette Promotion in New Zealand.

Principal Investigator:
Gaiser, J.
Objective:
To determine baseline data regarding public attitudes toward seven statements about smoking and health, with a view to recommending appropriate legislative action.
Methods or Approach:
In a survey that covered the 20 largest cities in New Zealand, a sample of 1,100 males and 1,100 females (aged 16 years or over) were interviewed. Calls were made at randomly designated homes where face-to-face interviews were conducted with the respondent. Callbacks were made at homes that were empty at first call to prevent interviewing only stay-at-home types. Fieldwork was completed during 1 week in February 1984. Questionnaires were checked, coded, and entered on data cards for computer processing.
Results to Date:
Results show that 87 percent of persons surveyed agree that children and young people should be strongly discouraged from ever taking up smoking (including 75 percent of smokers who do not want to stop smoking), and 81 percent agreed that the sale of cigarettes to children under 16 years of age should be banned. A slightly lower proportion (75 percent) agreed that the tax on cigarettes should be used to finance public education campaigns on the damaging effects of smoking on health and that smoking should not be allowed in enclosed public places. Among smokers who did not want to quit, the proportions were 52 percent and 46 percent, respectively. On the question of support for a ban on cigarette advertising, 53 of the total cohort agreed; however, only 25 percent of smokers who do not want to quit were in agreement compared with 60 percent of nonsmokers. When asked whether they would agree to sponsorship of sport and cultural events by cigarette companies, but only if no cigarette brand names are shown or mentioned, only 39 percent agreed (43 percent nonsmokers, 22 percent smokers who do not want to quit). Only 24 percent of participants agreed that advertising and sponsorships currently used by cigarette companies imply that smoking is helpful to success (17 percent smokers who do not want to quit, 28 percent of nonsmokers).
Future Plans:
The survey may be repeated after 5 years.
Project Dates:
February 1984.
Financial Support:
Cancer Society of New Zealand.

0404. NATIONAL HEART FOUNDATION OF NEW ZEALAND, PRINCESS MARGARET HOSPITAL, Cashmere Road, Christchurch 2, New Zealand.

Project Title:
Cigarette Smoking in New Zealand - Analysis of 1981 Population Census Results.

Principal Investigator:
Hay, D.R.
Objective:
To analyze results of the 1981 New Zealand population census concerning smoking habits; compare results with previous data from the 1976 population census.
Methods or Approach:
Results for 1981 were compared with those of 1976 and applied to various ethnic and social groups.
Results to Date:
Since 1976, the proportion of cigarette smokers has declined from 40 percent to 35 percent in men and from 32 percent to 29 percent in women. In men, there has been a reduction of smoking in every age group, but in women, smoking has increased in those aged 20 to 24 and 70 to 74 years. In adolescents (15 to 19 years of age) more girls than boys are smokers. Half of male and a third of female smokers consume ≥20 cigarettes/day. Smoking rates among Maori are much higher than among other ethnic groups; among Maori women aged 20 to 24, 70 percent are smokers. In all occupational groups, the proportion of smokers decreased between 1976 and 1981. Half as many professional workers are smokers (21 percent) compared with service workers (42 percent). The unemployed have the highest proportion of smokers; 56 percent of the men and 52 percent of the women. The proportion of smokers is also higher with lower educational level. Among male doctors, the number of smokers has fallen from 20 percent in 1976 to 15 percent in 1981; among female doctors, rates declined from 17 percent to 13 percent. There has also been a reduction in smoking among nurses; 49 percent to 39 percent in men and 36 percent to 31 percent in women.
Future Plans:
If the 1986 census includes a question on smoking, future trends will be monitored.
Project Dates:
1982–1984.
Financial Support:
National Heart Foundation of New Zealand.
References:
(1) Hay, D.R.; Foster, F.H. "Intercensal Trends in Cigarette Smoking in New Zealand. 1. Age, Sex, and Ethnic Status." *New Zealand Medical Journal* 97(752):283-285, 1984. (2) Hay, D.R.; Foster, F.H. "Intercensal Trends in Cigarette Smoking in New Zealand. 2. Social and Occupational Factors." *New Zealand Medical Journal* 97(752):395-398, 1984. (3) Hay, D.R. "Intercensal Trends in Cigarette Smoking by New Zealand Doctors and Nurses." *New Zealand Medical Journal* 97(754):253-255, 1984.

0405. UNIVERSITY OF OTAGO, MEDICAL SCHOOL, Wellcome Medical Research Institute, P.O. Box 913, Dunedin, New Zealand.

Project Title:
Continuing Survey of Factors Related to Cardiovascular Disease in Milton, A Small New Zealand Town.

Principal Investigator:
Simpson, F.O.
Objective:
To measure blood pressure, height, weight, 24-hour urinary sodium and other cardiovascular risk factors in the population; determine smoking and alcohol consumption patterns.
Methods or Approach:
Surveys were conducted in 1975, 1978, and 1981. The 1985 survey is under way. It is noted that smoking data forms only a small part of the project.
Results to Date:
Alcohol consumption and cigarette smoking were related in both men and women. Headache was weakly associated with cigarette smoking in women but not in men.
Financial Support:
National Heart Foundation of New Zealand; MRC, New Zealand.
References:
(1) Paulin, J.M.; Waal-Manning, H.J.; Simpson, F.O., et al. "The Prevalence of Headache in a Small New Zealand Town." *Headache* (In press). (2) Paulin, J.M.; Simpson, F.O.; Wall-Manning, H.J. "Alcohol Consumption and Blood Pressure in a New Zealand Community Study." *New Zealand Medical Journal* (In press).

NIGERIA

0406. UNIVERSITY COLLEGE HOSPITAL, Departments of Internal Medicine and Community Health, Ibadan, Oyo State, Nigeria.

Project Title:
The Pattern of Cigarette Smoking Among Students in Institutions of Higher Learning in Nigeria.

Principal Investigators:
Onadeko, B.O.; Awotedu, A.A.; Onadeko, M.O.
Objective:
To determine the prevalence of smoking among post-high-school students (male and female).
Methods or Approach:
There is no authentic record of smoking habits from this group of students; early surveys concentrated mainly on secondary (high) school students, except one survey of 236 students in a medical school. This survey included two universities (all faculties), two polytechnical schools, two colleges of education, and two schools of nursing. Both male and female students were selected and bias was excluded as much as possible by explaining the purpose of the study. Questionnaires were completed in lecture rooms and collected immediately; anonymity of participants was assured. Over 3,000 students participated and more than 80 percent satisfactorily completed the questionnaire.
Results to Date:
There was a definite increase in smoking; 31 percent of male and 21 percent of female students who completed the questionnaire were smokers. Reasons given for smoking showed that parental example was not significant; most picked up smoking from friends and smoked to be sociable or to release tension. Teachers who smoked did not influence students. About 50

percent of smokers consumed < 10 cigarettes/day, are probably not addicted, and thus could be persuaded to stop. Most of the students, both smokers and nonsmokers, would welcome some form of antismoking legislation. Results will be published.

Future Plans:
Survey participants will be followed up to determine whether any students have quit smoking.

NORWAY

0407. NATIONAL COUNCIL ON SMOKING AND HEALTH, P.O. Box 8025 Dep., 0030 Oslo 1, Norway.

Project Title:
Smoking Habits of Norwegian Theologians (1982).

Principal Investigators:
Hauknes, A.; Haoy, S.
Objective:
To analyze smoking habits of Norwegian theologians; compare habits with those of other professionals and the general adult population.
Methods or Approach:
A representative sample of theologians received a mailed questionnaire in 1982 inquiring about past and present smoking habits and attitudes toward smoking. About 91 percent of the sample responded. There were only 50 responses from women, which were excluded from the figures reported.
Results to Date:
Among the 1,086 male theologians that responded, 8 percent smoked daily, the lowest rate yet recorded in any adult group in Norway. In the adult male population as a whole, 42 percent smoked daily (age-adjusted figures). However, the percentage of occasional smokers was relatively high among the theologians compared with the general male population; 21 percent for theologians, 10 percent (age-adjusted figures) for general population.
Project Dates:
1982–1983.
Financial Support:
National Council on Smoking and Health, Norway.

0408. NATIONAL COUNCIL ON SMOKING AND HEALTH, P.O. Box 8025 Dep., 0030 Oslo 1, Norway.

Project Title:
Smoking Habits of the General Population of Norway.

Principal Investigator:
Lochsen, P.M.
Objective:
To continue followup study of smoking habits of the general population of Norway.
Methods or Approach:
A representative, stratified sample of the total population, aged 16 to 74 years, includes approximately 2,500 persons who are members of households participating in a study of work reserves that is conducted on an annual basis. Smoking data are collected by personal interviews, and recent changes or efforts to quit smoking are recorded. The surveys are conducted in December of each year.
Results to Date:
The proportion of male smokers decreased between 1973 and 1983, from 51 percent to 42 percent, while the proportion of female smokers has remained steady; 32 percent in both 1973 and 1983. Smoking has decreased among men in all educational categories and in blue- and white-collar occupations.
Project Dates:
1973–continuing.
Financial Support:
National Council on Smoking and Health, Norway.

0409. NATIONAL COUNCIL ON SMOKING AND HEALTH, P.O. Box 8025 Dep., 0030 Oslo 1, Norway.

Project Title:
Smoking Habits of Norwegian Schoolchildren (1985).

Principal Investigators:
Lochsen, P.M.; Folgero, S.
Objective:
To (1) record incidence of smoking among schoolchildren; (2) analyze interpersonal influences on initiation of smoking; (3) study regional differences in smoking habits; and (4) encourage local and national interest in the smoking problem, particularly among teachers, parents, and the children.
Methods or Approach:
All Norwegian schoolchildren in grades seven through nine (aged 13 to 15 years) complete anonymous forms in class. A representative sample is put into envelopes that are sealed and returned to the National Council on Smoking and Health for statistical analysis. In addition, each teacher will be asked to count the number of current smokers, occasional smokers, and nonsmokers in the class, by sex. Results for each grade will be summarized in a school report that will be returned to the national council.
Results to Date:
Results will be compared with surveys conducted in 1975 and 1980; findings will be available early in 1986.
Project Dates:
1975–continuing.
Financial Support:
National Council on Smoking and Health, Norway.

0410. NATIONAL COUNCIL ON SMOKING AND HEALTH, P.O. Box 8025 Dep., 0030 Oslo 1, Norway.

Project Title:
Smoking Habits of Norwegian Doctors (1984).

Principal Investigators:
Lochsen, P.M.; Thurmer, H.
Objective:
To analyze smoking habits of Norwegian doctors; compare data with smoking habits of other professionals and the general adult population.
Methods or Approach:
The study is a followup to a similar survey conducted in 1974. A representative sample of Norwegian doctors received a mailed questionnaire in 1984 inquiring about past and present smoking habits and attitudes toward smoking. Questions on smoking habits were identical to questions used in the 1974 survey.

Results to Date:
Preliminary analysis suggests a strong reduction in smoking rates among doctors since 1974; findings will be reported in 1985.
Project Dates:
1984–1985.
Financial Support:
National Council on Smoking and Health, Norway.

0411. NATIONAL MASS RADIOGRAPHY SERVICE, P.O. Box 8155, Oslo Dep 1, Norway.

Project Title:
The Cardiovascular Disease Study in Norwegian Counties.

Principal Investigator:
Byartveit, K.
Objective:
To correlate smoking history with other cardiovascular risk factors and to study the relationship of smoking to mortality from various causes.
Methods or Approach:
Approximately 60,000 persons (aged 20 to 54 years) have been examined, most of them twice, in three Norwegian counties. Questionnaire data is recorded and blood pressure, height and weight, blood lipids, and blood glucose levels are measured. Multivariate analysis is used to investigate the incidence of various cancers and the relationship of cardiovascular risk factors with mortality.
Results to Date:
Results from the first screening have been published.
Future Plans:
A third round may be carried out in the three counties to collect followup data with respect to cause-specific mortality and cancer incidence.
Project Dates:
1974–continuing.
Financial Support:
Norwegian Government.
Reference:
Bjartveit, K.; Foss, O.P.; Gjervig, T. "The Cardiovascular Disease Study in Norwegian Counties. Results From First Screening." *Acta Medica Scandinavica* Supplement 675:1-184, March, 1983.

0412. NORWEGIAN RADIUM HOSPITAL, Laboratory for Environmental and Occupational Cancer, Montebello, N-0310 Oslo, Norway.

Project Title:
Effect of Cigarette Smoke Extract and Smokeless Tobacco on Cell Transformation.

Principal Investigators:
Sanner, T.; Rivedal, E.
Objective:
To study how cigarette smoke extract and smokeless tobacco affect cell transformation induced by different environmental and occupational carcinogens.
Methods or Approach:
Morphological transformation of cells is studied using Syrian hamster embryo cells derived from cryopreserved primary cultures. Cocarcinogenic effects of cigarette smoke extract, snuff, and chewing tobacco are studied by coexposure with known carcinogens. Ability of substances to initiate and promote cell transformation is studied by use of a recently developed sequential exposure procedure.
Results to Date:
Cigarette smoke extract induced morphological transformation of cell colonies and enhanced transformation ability of several other carcinogens. Cigarette smoke extract acted primarily as a promoter.
Project Dates:
July 1979–July 1987.
Financial Support:
Norwegian Radium Hospital; Norwegian Cancer Society.

0413. TELEMARK SENTRALSJUKEHUS, Department of Occupational Medicine, Olavsgt. 26, 3900 Porsgrunn, Norway.

Project Title:
Cohort Study of Asbestos-Related Illnesses in Workers Previously Exposed to Asbestos in a Saltpeter Plant.

Principal Investigators:
Hilt, B.; Langard, S.; Rosenberg, J.
Objective:
To (1) investigate the effects of occupational exposure to asbestos in a saltpeter plant located in southern Norway; (2) contribute to the design and justification of screening programs for former asbestos workers; and (3) further knowledge on dose–response and dose–effect relationships.
Methods or Approach:
The study is designed as a retrospective and prospective mortality and morbidity cohort study of all men who were directly and indirectly exposed to asbestos dust in two divisions of the plant and who started work there between 1929 and 1970 (about 320 persons). The cohort is divided into subgroups on the basis of assumed different levels of exposures. Most of the 160 men still living have been subjected to a medical examination which also includes a chest X-ray and simple spirometry. A detailed work history is taken from every man and respiratory symptoms are registered on a questionnaire (Medical Research Council, 1976). The cohort is followed up by yearly examinations for at least 5 years. Occupational data on the deceased members of the cohort are obtained from the plant's personnel department. Health data are obtained from the plant's medical department, from the local hospital, and from the Norwegian Cancer Registry. Data on smoking habits are collected from different sources and taken into consideration in the statistical calculations.
Results to Date:
A study of the occurrence of cancer in a special subgroup of this cohort was published in 1981. The results of the clinical examinations have been published in an internal report (Telemark Sentralsjukehus, Department of Occupational Medicine, Report 81.05). A final report regarding cancer incidence in this cohort is being prepared for publication.
Project Dates:
January 1975–1984.
Financial Support:
Telemark Sentralsjukehus, Norway.
Reference:
Hilt, B.; Rosenberg, J.; Langaerd S. "Occurrence of Cancer in a Small Cohort of Asbestos-Exposed Workers." *Scandinavian Journal of Work and Environmental Health* 7:185-189, 1981.

0414. ULLEVAAL HOSPITAL. Medical Outpatient Clinic, Oslo I, Norway. OSLO DEPARTMENT OF HEALTH AND LIFE INSURANCE COMPANIES, Institute of Medical Statistics, Oslo, Norway.

Project Title:
Effect of Diet and Smoking Intervention on the Incidence of Coronary Heart Disease.

Principal Investigators:
Hjermann, I.; Velve Byre, K.; Holm, I., et al.
Objective:
To determine whether the lowering of blood lipids by dietary changes and cessation of smoking, if maintained for many years, would lead to reduction in the incidence of first attacks of coronary heart disease (CHD) in men aged 40-50 years.
Methods or Approach:
A total of 1,232 healthy, normotensive men at high risk of CHD submitted to a 5-year randomized trial. Men in the intervention group were counseled to lower their blood lipids by changing their diets and to stop smoking. Diagnosis of events of cardiovascular disease during the study was made blindly.
Results to Date:
Compared to the control group, the intervention group had 13 percent lower mean serum cholesterol during the trial; a 20 percent drop in mean fasting serum triglycerides; and a 45 percent greater decrease in tobacco consumption. Only 25 percent of the smokers in the intervention group stopped smoking completely, compared with 17 percent of the control group. At the end of the observation period, incidence of myocardial infarction and sudden death was 47 percent lower in the intervention group. When the incidence of strokes was added, the difference between the groups was still significant. Statistical analysis showed that the reduction in incidence in the intervention group is correlated with the reduction in total cholesterol and to a lesser extent with smoking reduction. Three years after finishing the controlled diet–antismoking trial, tobacco consumption was checked in the two groups. In the treatment group, consumption had increased, while among the controls, a significant decrease was noted. This resulted in an almost complete convergence of consumption levels. During the trial, participants met for intervention help every sixth month. After 5 years, there was no intervention.
Financial Support:
City of Oslo; Norwegian Council of Cardiovascular Diseases.
Reference:
Hjermann, I.; Velve Byre, K.; Holme, I., et al. "Effect of Diet and Smoking Intervention on the Incidence of Coronary Heart Disease: Report From the Oslo Study Group of a Randomized Trial in Healthy Men." *Lancet* 8259:1303-1310, 1981.

0415. UNIVERSITY OF BERGEN, Department of Obstetrics and Gynecology, Kvinneklinikken N-5016, Haukeland Sykehus, Bergen, Norway.

Project Title:
Smoking, Hemoglobin Levels, and Birth Weights in Normal Pregnancies.

Principal Investigators:
Nilsen, S.T.; Sagen, N.; Kim, H.C., et al.
Objective:
To study smoking habits and hemoglobin levels in relation to birth weight in Norwegian women in the last trimester of normal singleton pregnancies.
Methods or Approach:
Subjects were 811 healthy women who delivered newborns without congenital malformations after 37 weeks or more of pregnancy. Erythrocyte indices tested were hematocrit, red blood cell count, mean cell volume, mean cell hemoglobin, and mean cell hemoglobin concentration. Smoking habits, recorded by personal interview during second and third trimester, included number of cigarettes smoked/day. Infant birth weight was recorded during the first few minutes of life. Statistical analysis was performed by computer.
Results to Date:
Of the otherwise healthy women, 43 percent smoked during the third trimester. No significant association existed between smoking habits and hemoglobin levels during the third trimester, but the fairly small number of heavy smokers (>10 cigarettes/day) may have precluded discovery of subtle true differences. There was a strong correlation between smoking and low birth weight; 47 percent of newborn infants of heavy smokers were in the lowest quartile. Hemoglobin levels were inversely correlated to birth weight quartiles in smokers and nonsmokers; however, when birth weights were grouped according to maternal hemoglobin at term, the tobacco-related effect on birth weight appeared only with hemoglobin levels >12 g/dL, being particularly strong for levels >13 g/dL. Hemoglobin levels of 9.0 to 11.9 g/dL appeared to have a protective effect for fetuses of nonanemic mothers who smoked. Growth-retarded infants of smokers tended to be thin, indicating that they had been deprived of nutrients.
Reference:
Nilsen, S.T.; Sagen, N.; Kim, H.C., et al. "Smoking, Hemoglobin Levels, and Birth Weights in Normal Pregnancies." *American Journal of Obstetrics and Gynecology* 148(6):752-758, March 15, 1984.

0416. UNIVERSITY OF BERGEN, Department of Social Psychology, Oisteinsgate 3, N-500 Bergen, Norway. UNIVERSITY OF JYVASKYLA, Department of Health Sciences, Finland.

Project Title:
Health Behaviour in Schoolchildren. A WHO Cross-National Survey.

Principal Investigators:
Kannas, L.; Aaro, L.E.
Objective:
To (1) study health behavior (smoking habits) of schoolchildren in different European countries; (2) conduct cross-sectional and longitudinal comparisons between countries; (3) study personal and environmental factors related to health behavior (attitudes, images, subjective norms, social support); (4) analyze health behavior against sociodemographic factors; and (5) outline and discuss implications of findings for health education among young people in particular and for health promotion in general.
Methods or Approach:
A representative sample of schoolchildren in each country (aged 11, 13, and 15) will complete questionnaires in the classroom. Sample size will probably be about 3,000 in each country. Data collection will be carried out by teachers or other interviewers following a standard procedure that ensures anonymity. The survey will be conducted regularly, every second or third year. A core of questions on health behavior (smoking habits) is included in every survey, but an additional part has a special focus that changes from survey to survey. The first survey, carried out in 1983-1984 in Austria, England, Finland, and Norway, focused on smoking habits. The main focus in the 1985-1986 survey, which will be carried out in 8 to 10 European countries, will be on physical activity.

Results to Date:
Main findings of the 1983-1984 survey in Norway were that (1) smoking rates in all age groups are lower than in a 1980 survey; (2) prevalence of weekly smokers is very high among pupils planning to have a job after finishing basic school and is lowest among pupils planning higher theoretical education, a pattern that is similar for other health habits; (3) negative health behavior is strongly overrepresented among pupils reporting poor school achievement and those who don't like school; and (4) social network variables are confirmed as the most important predictors of smoking habits.
Project Dates:
January 1982–continuing.
Financial Support:
WHO.

0417. UNIVERSITY OF BERGEN, INSTITUTE OF HYGIENE AND SOCIAL MEDICINE, 5016 Haukeland Sykehus, Bergen, Norway.

Project Title:
Reproductive Experience and Cancer Risk.

Principal Investigators:
Bjelke, E.; Eide, G.E.
Objective:
To examine in detail the effects of reproductive experience on cancer occurrence and mortality from noncancer causes.
Methods or Approach:
Between 1956 and 1959, about 70 percent of women aged 20 to 69 in three counties in Norway attended a screening examination for breast cancer and responded to a questionnaire that elicited information on reproductive experience (parity, age at first birth, age at menarche, and age at menopause).
Results to Date:
In the cohort of 63,000 women, approximately 7,000 cases of cancer had been diagnosed by the end of 1980, more than 1,500 of these being breast cancer. Data on height, weight, and ABO blood group are being collected for a subgroup to evaluate possible confounding by the variables and to examine possible interactions with reproductive variables in relation to cancer occurrence.
Project Dates:
1956–continuing.
Financial Support:
NCI (N01CP91043); Norwegian Cancer Society; Norwegian Society for Fighting Cancer; University of Bergen.

0418. UNIVERSITY OF OSLO, INSTITUTE OF SOCIAL MEDICINE, Aker Hospital, Department of Gynecology and Obstetrics, 0514 Oslo 5, Norway.

Project Title:
Some Social Background Variables Among Smoking and Non-Smoking Primiparae.

Principal Investigators:
Dalaker, K.; Grunfeld, B.; Jansen, A.
Objective:
To determine the smoking habits in Norwegian primiparae in relation to age, marital status, occupation, and housing conditions.
Methods or Approach:
Subjects were Norwegian primiparae admitted to Aker Hospital in 1978 and 1979. Information on smoking habits and social background was based on routine antenatal care consultations carried out by general practitioners and/or personnel in the hospital's outpatient clinic, and from hospital records. Average number of cigarettes smoked/day was recorded on the standard questionnaire along with other relevant information. Housing was defined as "poor" when there was more than one person/room (excluding kitchen) and "good" when better conditions existed.
Results to Date:
Among the 2,427 primiparae, 62.7 percent were nonsmokers, 23.0 percent smoked <10 cigarettes/day, and 14.3 percent smoked ≥ 10 cigarettes/day. There was a significant correlation between smoking in pregnancy and age below 20 years, unmarried or previously married status, and poor education ($p<0.001$). Poor housing was of less importance. Mean age of smokers (24.0 years) was significantly lower than age of nonsmokers (25.8 years, $p<0.001$). Overall incidence of smoking in pregnancy was not significantly different from the normal population, but pregnant women under age 20 smoked significantly more and those over age 24 significantly less compared with their counterparts in a normal population ($p<0.01$).
Project Dates:
1981–1983.
Reference:
Dalaker, K.; Grunfeld, B.; Jansen, A. "Some Social Background Variables Among Smoking and Non-smoking Primiparae." *Scandinavian Journal of Social Medicine* 11:23-26, 1983.

0419. UNIVERSITY OF OSLO, INSTITUTE OF SOCIAL MEDICINE, Aker Hospital, Department of Gynecology and Obstetrics, 0514 Oslo 5, Norway.

Project Title:
Smoking in Pregnancy.

Principal Investigators:
Dalaker, K.; Grunfeld, B.; Jansen, A.
Objective:
To investigate importance of maternal age, marital status, occupation, and housing conditions in relation to smoking habits as explanatory variables for low birth weight; compare perinatal mortality and complications of pregnancy and delivery among smokers and nonsmokers.
Methods or Approach:
Information on all nulliparae admitted to Aker Hospital, Oslo, in 1978 and 1979 was collected during routine antenatal visits and from hospital records. Data on social background, smoking habits, and previous gynecologic and obstetric history was collected about the 30th week of pregnancy. Housing conditions were defined as "poor" when there was more than one person/room (excluding kitchen and bathroom) and "good" when better conditions existed. Gestational age at birth was assessed by (1) a pediatrician during the first day of life and (2) date of the last menstrual period (Naegele's formula). Only women with regular menstrual periods of less than 35 days were included.
Results to Date:
Among 2,427 primiparae, mean birth weight for infants of smokers was 160 g lower than for infants of nonsmokers, and the frequency of infants with birth weight $<2{,}500$ g was 75 percent higher among smokers. There was a positive correlation between low birth weight and maternal age below 20 years, unmarried status, poor housing conditions, and low educational level. The importance of smoking as a risk factor for reduced birth weight was independent of other social factors. Mean gestational age calculated from date of last menstrual period was somewhat shorter among mothers who smoked, but no difference was found at clinical estimation of

gestational age. Perinatal mortality was significantly more common among infants of mothers who smoked, particularly with regard to stillbirth caused by abruptio placentae. Abruptio placentae occurred more frequently among smokers, whereas the total proportion of complications of pregnancy and delivery were similar in smokers and nonsmokers.

Project Dates:
1981–1983.

Reference:
Dalaker, K.; Grunfeld, B.; Jansen, A. "Smoking in Pregnancy." *Journal of Oslo City Hospital* 34:21-27, 1984.

0420. UNIVERSITY OF TROMSO, INSTITUTE OF COMMUNITY MEDICINE, Storgt. 25, P.B. 417, N-9100 Tromso, Norway.

Project Title:
Tromso Heart Study.

Principal Investigators:
Thelle, D.; Forde, O.H.; Arnesen, E.

Objective:
To (1) assess established coronary risk factors in a male population aged 20 to 49 years; (2) examine relationship between risk factors and social and physical variables; (3) determine social and physical variables affecting future coronary heart disease (CHD); (4) determine importance of a positive family history of CHD in determining risk for future CHD; and (5) relate changes in incidence to changes in risk factor level over time.

Methods or Approach:
The study cohort consisted of 6,600 male subjects examined in 1974 and 16,664 men and women examined in 1979. All received a postal questionnaire concerning physical activity at work and at leisure, ethnic origin, smoking habits, and a number of social conditions. Blood pressure, serum lipids, height, weight, and hemoglobin level were measured. A register for coronary events has been established to ensure the prospective aspect of the project.

Results to Date:
Results suggest that the relatively high mortality from CHD in northern Norway is associated with high serum cholesterol concentrations and a relatively high prevalence of smoking. During screening there were indications of changes in dietary habits, presumably as a result of accompanying publicity. Differences in risk factors between subjects with positive and negative family history of myocardial infarction (MI) were surprisingly small. Correspondingly, there was no difference in frequency of MI relatives in subjects belonging to the upper and lower quintiles of serum cholesterol and blood pressure distribution. The slight elevations in serum cholesterol and blood pressure contribute very little to increased risk in subjects with positive family history.

Project Dates:
February 1974–continuing.

Financial Support:
University of Tromso; Norwegian Council on Cardiovascular Disease; Norwegian Research Council for Science and the Humanities.

0421. UNIVERSITY OF TRONDHEIM, Department of Botany, Pathology Laboratory, Section for Cell Biology, N-7055 Dragvoll, Norway.

Project Title:
Alveolar Macrophages From Expectorates - Biological Monitoring of Workers Expcsed to Occupational Air Pollution.

Principal Investigators:
Nilsen, A.; Gullvag, B.M.; Mylius, E., et al.

Objective:
To measure respiratory tract irritation caused by occupational air pollution (with/without smoking); develop biological monitoring method for alveolar macrophages (AM).

Methods or Approach:
To count AM from expectorates, a method was developed for obtaining reproducible results that has shown a dose–response relationship between exposure and number of AM. Different working sites and different airway protection equipment can be evaluated; results for smokers and nonsmokers can be separated. The Ames *Salmonella typhimurium* test is used.

Results to Date:
Both the AM test and Ames test show a strong synergistic effect between occupational air pollution and smoking. An earlier suggestion that occupational air pollution effects should be studied in nonsmokers may not be relevant, since there is a stronger effect on smokers, which is seen both for lung irritating agents (measured with the AM test) and for potential mutagens (measured by the Ames test).

Project Dates:
September 1978–December 1986.

Reference:
Nilsen, A.M. *Alveolar Macrophages From Expectorates - Biological Monitoring of Workers Exposed to Occupational Air Pollution. An Evaluation of the AM-Test.* Doctoral Dissertation, University of Trondheim, Norway, 1984, 142 pp.

0422. UNIVERSITY OF TRONDHEIM, Department of Botany, N-7055 Dragvoll, Norway.

Project Title:
Use of Expectorate for Measuring Carcinogenic/Mutagenic Load on Exposed Workers.

Principal Investigators:
Krokje, A.; Mylius, E.; Gullvag, B.

Objective:
To determine, with sputum samples, whether dust in the working environment contains mutagens that are available to the human body; determine whether smoking adds or has a synergistic effect on load of occupational mutagens.

Methods or Approach:
The Salmonella/mammalian-microsome mutagenicity test was used on sputum samples from exposed workers and controls, both smokers (10 cigarettes/day, ≥ 1 year) and nonsmokers (never smoker or ex-smoker for at least 2 years). People who did not fit these categories were excluded from the study. Participants were instructed to cough three times. Material was pooled for the different groups, hydrolyzed with alkaline methanol, and extracted by cyclohexane. Mutagenic activity was assayed by the Ames plate incorporation method.

Results to Date:
Sputum from exposed workers (mostly smokers, but some nonsmokers) were mutagenic; samples from controls (smokers and nonsmokers) were not. Results suggest a synergistic relationship between exposure to air pollution in the workplace and smoking. The positive response in exposed smokers and negative response of control smokers may be because mutagens in cigarette smoke are present in small amounts compared with presence of comutagens in smoke. In addition, exposure to cigarette smoke may result in a decrease in mucociliary clearance and, thus, in accumulation in the respiratory tract of particles possessing adsorbed mutagens.

Future Plans:
Liver homogenates from rats were used as metabolic activation

system; in the future, lung homogenates will also be used. The mutagenicity of sputum given at different periods after exposure (working environment or smoking) will be studied.

Financial Support:

Norwegian Council for Scientific and Industrial Research.

0423. VESTFOLD CENTRAL HOSPITAL, Departments of Pediatrics and Clinical Laboratory, 3100 Tonsberg, Norway.

Project Title:

Smoking During Pregnancy - Effects on the Thyroid Function of the Fetus.

Principal Investigators:

Meberg, A.; Marstein, S.

Objective:

To evaluate the status of the thyroid at birth in newborn infants of mothers who smoked during pregnancy.

Methods or Approach:

One of the main detoxification products from the cyanide content in tobacco smoke is known to have thyreostatic effects. It was hypothesized that the fetus might have a biochemical condition of latent hypothyreosis at birth. Two groups of pregnant women were studied: 50 subjects who had smoked ≥ 10 cigarettes/day during pregnancy and 50 nonsmokers. At birth, umbilical cord blood was sampled for measurements of T-4, TSH, T-r, R-T-4, and thiocyanate concentration. Findings will be correlated with smoking habits (cigarettes/day) and thyroid parameters correlated with serum thiocyanate levels.

Results to Date:

Results are not yet available.

Project Dates:

July 1984–February 1985.

Financial Support:

Vestfold Central Hospital.

PAKISTAN

0424. K.V. SOCIAL SECURITY SITE HOSPITAL, Manghopir Road, Karachi-16, Pakistan.

Project Title:

Tobacco Chewing and Oropharyngeal Cancer.

Principal Investigator:

Beg, M.H.A.

Objective:

To determine site of oral cavity lesions and relationship with frequency of chewing and duration of keeping the quid at the site; study frequency and involvement of pharyngeal sites in relation to tobacco chewing.

Methods or Approach:

Complete histories are obtained to determine basic data, including type of tobacco used, frequency of chewing, and whether the quid is kept in the mouth at night. Otolaryngological examination includes fiberoptic examination under local anesthesia to determine site, extent of lesion, and TNM classification. Lesions are coded according to international classification (WHO 1976).

Results to Date:

Tobacco is commonly chewed in pan (betel leaves), and the habit is more common among those who migrated to the area after partition of India in 1947. There appears to be a definite relationship between tobacco chewing and sites of lesions in the oral cavity and pharynx. The most common site in the oral cavity is cheek mucosa, and in the pharynx, the valecula and pyriform fossa. Lesions are more common in male immigrants between the ages of 41 and 50 years.

Future Plans:

Plans are to continue the project using animals, and applying various types of tobacco to determine the kind of tobacco most likely to cause malignancy.

Project Dates:

January 1976–December 1985.

0425. KHYBER MEDICAL COLLEGE, Department of Dentistry, Peshawar, Pakistan.

Project Title:

The Incidence of Oral Leukoplakia and Related Lesions in Naswar Addicts.

Principal Investigator:

Khadim, M.I.

Objective:

To determine the relationship between oral leukoplakia or other keratotic lesions and use of naswar; determine incidence of other orodental diseases in naswar addicts.

Methods or Approach:

Naswar is an indigenous preparation of powdered tobacco and wood ash or calcium hydroxide. It is kept in the mouth (in the vestibule against the lower incisors and canine teeth) for 5 to 20 minutes several times a day for as long as 50 to 60 years. Oral mucosa of patients attending dental clinics is carefully examined and leukoplakia is diagnosed.

Results to Date:

Tobacco, a major ingredient of naswar, is thought to be responsible for the high incidence of cancer and precancerous conditions of the oral mucosa in India and other countries in Southeast Asia. Data show that 10 of 1,200 (0.83 percent) of naswar addicts exhibit leukoplakia, which probably reflects only a fraction of actual prevalence, partly because of ignorance as to the significance of white lesions in the oral mucosa. Also, since the disease is not painful, most people do not seek treatment until lesions undergo malignant transformation. The project has been modified to incorporate information on use of naswar so that it will now be possible to determine the correlation of cancerous or precancerous lesions of the oral cavity and use of naswar.

Future Plans:

Steps will be taken to prevent leukoplakia and other related lesions.

Project Dates:

November 1979–November 1984.

Financial Support:

Khyber Medical College, Peshawar, Pakistan.

0426. COPERNICUS ACADEMY OF MEDICINE, Department of Pneumonology, Shawinska 8, 31-066 Krakow, Poland.

Project Title:
Value and Limits of the Bacteriological Study of Biopsy Specimens and Bronchial Washing in Smoking and Nonsmoking Patients with Pulmonary Disease.

Principal Investigators:
Owsinski, J.M.; Zawadzka, S.; Klisiewicz-Panszczyk, T.

Objective:
To determine differences in bacteriological flora from bronchial washings and biopsy specimens from bronchial mucosa taken by bronchoscope or bronchofiberoscope, from patients with pneumonia, bronchitis, bronchiectasis, lung cancer, and other pulmonary diseases.

Methods or Approach:
The normal techniques of bronchoscopy or bronchofiberoscopy are used to obtain bronchial washings and specimens of bronchial mucosa taken by forceps. Data obtained in the bacteriological laboratory are compared with data on cigarette smoking and other clinical findings. It is anticipated that results from specimens of bronchial mucosa will be more valuable than bronchial washings, which are contaminated by bacteria from the upper respiratory tract and pharynx. Bronchial mucosa should contain only possible pathogens of the lower respiratory tract.

Results to Date:
Project is in a preliminary phase.

Project Dates:
January 1985–December 1986.

Financial Support:
Copernicus Academy of Medicine.

0427. COPERNICUS ACADEMY OF MEDICINE, Department of Pneumonology, Skawinska 8, 31-066 Krakow, Poland.

Project Title:
Influence of Urban Factors on the Incidence of Chronic Bronchitis in Rural Populations.

Principal Investigators:
Nikodemowicz, E.; Owsinski, J.M.; Chomicka, Z., et al.

Objective:
To determine whether urbanization contributes to higher incidence of chronic bronchitis.

Methods or Approach:
Two suburban villages (total population 2,192), located 2 to 4 km from the city of Lancut, were selected. Atmospheric pollution (concentration of dusts) averages 11 mg/m^3 (maximum 22 mg/m^3); average sulfur dioxide concentration is 8 mg/m^3 (maximum 33 mg/m^3). Two control villages (total population 2,791) are located 20 to 25 km from the city. Atmospheric pollution (dust concentration) averages 8 to 10 mg/m^3; SO_2 averages 6 mg/^{3} (maximum 15 mg/m^3). Only people over 18 years of age were examined; 1,265 in suburban villages, 1,608 in rural villages. Questionnaires were used to collect standard data and included questions concerning specific work and social conditions of farmers. Statistical evaluation was based on chi-square test with Yates correction at a significance level of $p < 0.05$.

Results to Date:
In the combined village populations, 1,784 were nonsmokers (66.6 percent), 111 were ex-smokers (4.1 percent), and 784 (29.3 percent) were current smokers (55.3 percent male, 5.8 percent female). Chronic bronchitis was found more often in suburban inhabitants (6.7 percent) than in rural inhabitants (4.4 percent), a significant difference. Among smokers, the difference in chronic bronchitis incidence was also significant: 11.7 percent for urban and 6.3 percent for rural dwellers. It is concluded that chronic bronchitis is twice as common in the city as in rural areas; however, in both environments cigarette smoking and air pollution lead to higher incidence.

Future Plans:
In continuing investigations, examinations will include x ray, anthropometric and spirometric tests, blood pressure readings, and electrocardiographs. Observation of groups with and without chronic bronchitis is planned.

Project Dates:
1978–December 1988.

Financial Support:
Copernicus Academy of Medicine, Poland.

Reference:
Nikodemowicz, E.; Owsinski, J.; Czajka, S., et al. "Influence of Urban Factors on the Incidence of Chronic Bronchitis in Rural Populations." *Polskie Archiwum Medycyny Wewnetrznej* (Polish, English summary) (In press).

0428. COPERNICUS ACADEMY OF MEDICINE, Departments of Pnemonology and Pathology, Skawinska 8, 31-066 Krakow, Poland.

Project Title:
Bronchoalveolar Lavage in Pulmonary Diseases: Present Value and Limits.

Principal Investigators:
Chlap, Z.; Nikodemowicz, E.; Owsinski, J.M., et al.

Objective:
To study and analyze quantitatively the morphological and functional characteristics of cellular populations collected by bronchoalveolar lavage (BAL) as reflections of the physiopathological disorders occurring in the distal air spaces.

Methods or Approach:
In the washing technique used (Reynolds), 0.9 percent saline solution is injected into a segment or subsegmental territory through the bronchofiberscope located in the corresponding bronchus. The solution, collected immediately by gentle aspiration, contains a suspension of free cell populations from the walls of distal bronchi and alveoli and diluted secretions from peripheral pulmonary spaces. Studies were conducted on patients with lung cancer, chronic bronchitis and emphysema, sarcoidosis, pneumoconiosis, asthma, and pneumonia. Biochemical investigations were carried out of supernatant fractions (α_1-antitrypsin and immunoglobulins).

Results to Date:
Value of data obtained by BAL is linked to the technique, and numerous factors must be taken into account in interpreting results, including homogeneity of pulmonary lesions, stage of evolution and possible intervention of associated exogenous aggressions, and smoking habits. In nonsmokers, free cell population is 80 to 90 percent alveolar macrophages and 10 to 15 percent lymphocytes. In smokers, lymphocytes are reduced by 5 to 7 percent by the increase in alveolar macrophages. Repeated BAL can be used to follow evolution of diseases.

Project Dates:
March 1985–December 1989.

Financial Support:
Copernicus Academy of Medicine, Poland.

0429. INSTITUTE OF IMMUNOLOGY AND EXPERIMENTAL THERAPY, Department of Clinical Immunology, Czerska 12, 53-114 Wroclaw, Poland.

Project Title:
Effect of Smoking on Immunological Abnormalities in Asbestos Workers.

Principal Investigator:
Lange, A.
Objective:
To investigate effects of smoking on incidence of non-organ-specific autoantibodies, serum immunoglobulin levels, and delayed hypersensitivity to recall antigens in asbestos workers.
Methods or Approach:
Workers employed in an asbestos textile factory are followed for presence of lung diseases and immunologic abnormalities related to asbestos exposure with routine medical examinations that include chest x ray, ventilatory lung function, and autoantibody determination. During one of the surveys, skin reactivity to SK-SD, PPD, and PHA was evaluated. Cases showing abnormalities are admitted to the hospital for more detailed medical examination and immunologic workup (serum immunoglobulin and complement study, and skin reactivity to recall antigens). Data, collected by standard questionnaire, are processed with a computer program.
Results to Date:
Asbestos exposure induces higher levels of serum immunoglobulins, higher incidence of antinuclear antibodies (ANA), and impairment of skin reactivity to recall antigens. All abnormalities are positively correlated with symptoms of lung fibrosis. Preliminary data indicate lack of additive effect of smoking on immunological abnormalities in asbestos workers. Serum immunoglobulin G was less elevated in smokers than in nonsmokers. In addition, the fraction of workers showing presence of ANA at least one time during 8 years of observation was slightly lower in both male and female smokers. Nonsmoking males contributed more frequently to the group of asbestos workers who showed impairment of skin reactivity to recall antigens and phytohemagglutinin.
Future Plans:
The pattern of immunologic abnormalities in smoking and nonsmoking workers will be investigated and incidence and rate of progress of asbestos-related lung diseases will be followed in smokers and nonsmokers with/without immunologic abnormalities.
Project Dates:
January 1980–December 1988.
Financial Support:
Polish Academy of Sciences (10.5).

0430. INSTITUTE OF IMMUNOLOGY AND EXPERIMENTAL THERAPY, Department of Clinical Immunology, Czerska 12, 53-114 Wroclaw, Poland.

Project Title:
Effect of Adsorption of 3-Methylcholanthrene Onto Chrysotile Fibres of Aryl Hydrocarbon Hydroxylase Inducement in Mice.

Principal Investigator:
Lange, A.
Objective:
To investigate the carrier function of chrysotile fibers if coated with 3-methylcholanthrene (3-MC) in inducement of aryl hydrocarbon hydroxylase (AHH) in mice.
Methods or Approach:
Mice responsive to AHH inducement (C57BL/6JBoyIiw) and nonresponsive mice (NZB/Iiw) and their hybrids were injected i.p. with microcrystalline 3-MC, chrysotile fibers, 3-MC absorbed onto chrysotile fibers, and 3-MC dissolved in linseed oil (positive control). AHH activity level was measured fluorometrically in liver homogenates 4 days after injection.
Results to Date:
3-MC dissolved in oil induced significant increases in AHH activity in responsive mice and their F1 hybrids. No inducement was observed when chrysotile fibers or microcrystalline 3-MC were injected alone. However, 3-MC absorbed onto asbestos induced an increase in level of AHH activity in male C57BL/6 mice and male (NZB x C57BL/6)F1 mice in spite of the lack of oil solvent. In female mice, results varied between experiments, which seems due to chrysotile-dependent abrogation of AHH activity seen in some experiments.
Project Dates:
January 1982–December 1983.
Financial Support:
Polish Academy of Sciences (10.5).

0431. INSTITUTE OF INTERNAL MEDICINE, Hematological Clinic, Kopernika Strasse 17, Krakow, Poland.

Project Title:
Effect of Smoking on the Immune System.

Principal Investigator:
Lisiewicz, J.
Objective:
To prepare an article reviewing the effect of smoking on the immune system.
Methods or Approach:
The review, to be published in *Postepy Higieny i Medycyny Dosviadczalnej* is considered necessary to combine information published in various journals from other countries. It is anticipated that more than 100 references will be included.
Results to Date:
Preparation is almost complete. There is also a possibility of an English translation being made available.

0432. INSTITUTE OF ONCOLOGY, Armii Czerwonej 15, 44-101 Gliwice, Poland.

Project Title:
Lung and Larynx Cancer in Relation to Tobacco and Alcohol Consumption and Occupational Factors.

Principal Investigators:
Zemla, B.; Banasik, R.; Wojcieszek, Z.
Objective:
To determine risk of lung and laryngeal cancer in the Upper Silesian region of Poland, particularly in relation to tobacco use, alcohol consumption, and occupation; develop a mathematical model that will include all known risk factors for lung and laryngeal cancer.
Methods or Approach:
In the case–control study, incident cases and controls will be interviewed at the Institute of Oncology in Gliwice. To date, 328 cases of laryngeal cancer and 160 cases of lung cancer have been identified and 650 controls have been selected.
Results to Date:
A significant correlation between cigarette smoking and laryngeal cancer was found in 272 cases occurring in males in the heavily industrial region of Upper Silesia that appeared to be independent of smoking duration or intensity. Incidence was also higher among men who smoked cigars or pipes than

in nonsmokers. Exposure to various gases and dusts in the work environment seemed to influence cancer risk; however, almost all exposed workers also smoked.

Future Plans:
It is anticipated that by 1987, 500 laryngeal cancer cases and 500 lung cancer cases will have been interviewed, along with 2,000 controls.

Project Dates:
January 1984–October 1987.

Financial Support:
Polish Government (PR-6 0103).

Reference:
Zemla, B.; Wojcieszek, Z. "The Epidemiological Risk Factors of the Larynx Cancer Among the Native and Migrant Male Population." *Neoplasma* 31(4):465-474, 1984.

0433. KRAKOW MEDICAL ACADEMY, INSTITUTE OF SOCIAL MEDICINE, Department of Epidemiology, Kopernica 7, 31-034 Krakow, Poland.

Project Title:
Long Term Analysis of Cancer Mortality Among Krakow Inhabitants in Relation to Demographic and Environmental Factors.

Principal Investigators:
Jedrychowski, W.; Cholewka-Cabaj, K.

Objective:
To make comparisons among different types of cancer (especially lung and breast cancer) in relation to degree of air pollution exposure, smoking habits, fertility, and other epidemiological factors.

Methods or Approach:
Spatial analysis of mortality due to malignant neoplasms in the population of Krakow will cover the 10-year period from 1974 to 1984. The city of Krakow has over half a million inhabitants and its four districts differ in regard to degree of air pollution, smoking habits, fertility, and other social and environmental factors. A comparison will be made between mortality from malignant neoplasms in the four districts. Death certificates, collected monthly, are analyzed for cancer mortality data according to sex, place of residence, and primary site. Age-specific and age-adjusted rates will be computed for the total population and for each district.

Results to Date:
Analysis of 5-year data (1974 to 1978) showed that the highest specific mortality rates were due to cancers of the lung (30.3 percent); stomach (21.9 percent); liver, gallbladder, and pancreas (18.7 percent); colon and rectum (16.1 percent); and breast (14.0 percent). In males, the main causes of mortality were cancers of the lung (56.2 percent); stomach (27.4 percent); and liver, gallbladder, and pancreas (18.7 percent). In females, the main causes were cancers of the breast (26.6 percent), stomach and liver (22.5 percent), gallbladder (22.5 percent), and pancreas (22.5 percent). Data also show that mortality rates were higher in the city than in the suburbs.

Project Dates:
1974–1984.

0434. NATIONAL INSTITUTE OF HYGIENE, Department of Medical Statistics, Chocimska 24, 00-791 Warsaw, Poland.

Project Title:
Follow-up Study of Chronic Nonspecific Respiratory Diseases in Krakow.

Principal Investigators:
Wysocki, M.; Jedrychowski, W.; Krzyzanowski, M.

Objective:
To (1) estimate changes in chronic nonspecific respiratory symptoms and spirometric values over a 13-year observation period; (2) assess relationship of changes with smoking, air pollution, past illnesses, occupational exposures, and other possible risk factors; and (3) estimate role of ventilatory impairment and other respiratory symptoms as predictors of 13-year mortality.

Methods or Approach:
In 1968, randomly selected permanent residents (4,355 males and females aged 19 to 70 years) in Krakow were interviewed using a modified version of the MRC questionnaire. In over 70 percent, spirometric and anthropometric measurements were also taken. Two followup examinations were performed (1973 and 1981). Data from all three interviews were collected for 2,958 persons; in 1,746, spirometric tests were also performed. Among those examined in 1968, 523 died before 1981 and 261 were lost to followup. Cause of death was established through death certificates. Multiple logistic models were used in data analysis.

Results to Date:
The best predictors of forced expiratory volume in 1 sec (FEV_1) after 13 years were baseline level of ventilatory capacity and age. Regular smoking clearly decreased expected level of lung function and a beneficial effect of smoking reduction was not observed. However, an increase in number of cigarettes smoked/day had an unfavorable influence on FEV_1 in regular smokers. An index of risk of obstructive pulmonary disease was developed. In men, risk was related to number of cigarettes smoked. Cigarette smoking was also an important predictor of 13-year mortality in men, although this effect was not observed for cancer mortality. Level of respiratory function, which was related to cigarette smoking, was also an important predictor of mortality.

Future Plans:
The relationship of respiratory wheezing to lung function and other respiratory symptoms will be analyzed.

Project Dates:
March 1980–1985.

Financial Support:
NHLBI (P-05-109-N).

0435. NATIONAL RESEARCH INSTITUTE FOR MOTHER AND CHILD, Rabka Branch, ul. Parkowa 2, PL-34-410 Rabka, Poland.

Project Title:
Epidemiological Study of Long-Term Effects on Health of Air Pollution in Children.

Principal Investigators:
Rudnik, J.; Herman, S.M.; Pisiewicz, K., et al.

Objective:
To investigate relationship between chronic exposure to air pollution and indices of chronic respiratory diseases in children living under different social and domestic conditions; assess significance of various exogenous factors (including passive tobacco smoking) on development of the respiratory system.

Methods or Approach:
Two areas with contrasting levels of air pollution (the industrialized, highly polluted city of Krakow, and the small clean town of Limanowa) were studied, utilizing a linked cross-sectional design. In 1974, children aged 8 to 10 years were examined. In two successive examinations (1977 and 1980) children were reexamined and new groups of children were

added. Self-administered questionnaires, completed by the parents for each child, contained questions on present and past history of respiratory symptoms and diseases and on socioeconomic and housing conditions. In physical examinations, body weight and height were determined and lung function was tested. Standard lung function test was peak expiratory flow rate, but in subgroups, forced vital capacity and forced expiratory volume in 1 sec were also measured.

Results to Date:

In the three rounds, 15,114 observations were made on 12,708 children 8 to 16 years of age. Frequencies of all respiratory indices were significantly higher, and mean standardized lung function values were significantly lower, in children from the polluted area (in spite of better general physical development) than in children from the low pollution area. Two-thirds of the children lived in households with one or more adults who smoked. Prevalence of smoking was similar in the two areas; 67.3 percent in Krakow and 62.8 percent in Limanowa. Frequency of respiratory indices was uniformly higher, but not statistically significant, in children living together with smoking co-tenants. However, a combination of the two possible risk factors (living with tobacco smokers and with persons with chronic respiratory diseases) had a negative synergistic effect. In such children, frequency of respiratory symptoms and past respiratory diseases was significantly increased, especially cough, shortness of breath, and recurrent bronchitis.

Future Plans:

A followup study is planned of approximately 2,000 children (now young adults) from the main study who live in Krakow. Annual examinations will begin in 1985 and will continue for at least 10 years to assess the relationship between history of respiratory diseases in early childhood and functional status of the respiratory system and development of chronic respiratory conditions in adult life.

Project Dates:

April 1972–1995.

0436. PROVINCIAL BLOOD DONATION CENTRE AND PROVINCIAL UNION HOSPITAL, Ulica Jagiellonska 66, 25-956 Kielce, Poland.

Project Title:

Physiological and Biochemical Blood Parameters in Non-Smokers and Cigarette Smokers.

Principal Investigators:

Bartelik, S.; Ziolo, H.; Bartelik, M.

Objective:

To determine effect of cigarette smoking on blood serum proteins and lipids, hematological tests, and some hemostatic parameters.

Methods or Approach:

Analyses were performed in 20 nonsmokers and 20 smokers (>20 cigarettes/day). Subjects were males aged 22 to 30 years.

Results to Date:

In cigarette smokers, blood serum IgA, IgG, IgM, total lipids, and beta-lipoproteins were significantly decreased, while LC, packed cell volume, and alpha-2-macroglobulin were significantly increased.

Project Dates:

September 1982–June 1983.

Financial Support:

Provincial Blood Donation Center and Provincial Union Hospital, Poland.

Reference:

Bartelik, S.; Ziolo, H.; Bartelik, M. "Fizjologiczne i Biochemiczne Parametry Krwi Osob Niepalacych i Palacych Papierosy." *Polski Tygodnik Lekarski* 39(1):7-8, 1984.

0437. PROVINCIAL BLOOD DONATION CENTRE, Ulica Jagiellonska 66, 25-956 Kielce, Poland.

Project Title:

Protein Concentrations in Mixed Saliva of Children From Families of Nonsmokers and Smokers.

Principal Investigator:

Bartelik, S.

Objective:

To investigate effect of inhalation of atmospheric pollutants (from smoke of tobacco products) on concentrations of several proteins in mixed saliva.

Methods or Approach:

Material consists of mixed saliva of 13-year-old children, 27 from nonsmoking families and 28 (passive smokers) from families with tobacco smokers. Protein concentrations were determined by single radial immunodiffusion method.

Results to Date:

In mixed saliva of passively smoking children, concentrations of immunoglobulin (Ig)G, IgA, IgM, α_1-antitrypsin, and transferrin were lower; concentration of α_2-macroglobulin was higher. Differences were more pronounced in boys than in girls.

Project Dates:

April 1984–September 1984.

Financial Support:

Provincial Blood Donation Centre, Poland.

0438. UNIVERSITY MEDICAL SCHOOL, INSTITUTE OF INTERNAL MEDICINE, Hematological Clinic, Kopernika Str. 17, Krakow, Poland.

Project Title:

Effect of Industrial Noise on the Immune System in Smokers and Nonsmokers.

Principal Investigator:

Lisiewicz, J.

Objective:

To establish whether there are differences in human immune system changes between smokers and nonsmokers exposed to industrial noise.

Methods or Approach:

Numerous immunological tests will be conducted on about 100 workers (mostly men) of an industrial establishment. The control group will comprise about 50 men of the same age. E and EAC rosette tests will be used, and levels of immunoglobulins G, A, M, D, and E in serum will be determined. Other methods will include the NBT test, skin tests of delayed hypersensitivity, and myeloperoxidase, acid phosphatase, and beta-glucuronidase in peripheral blood neutrophils.

Results to Date:

Results are not yet available.

Project Dates:

October 1984–May 1985.

Financial Support:

University Medical School, Krakow, Poland.

PORTUGAL

0439. FACULTY OF MEDICINE OF LISBON, Department of Biochemistry, Av. Egas Moniz, 1600 Lisbon, Portugal.

Project Title:
Influence of Substances Inhaled From Tobacco Smoke on the Oxygen Affinity of Haemoglobin and on the Erythrocyte Deformability.

Principal Investigator:
Freitas, J.P.
Objective:
To determine influence of acute tobacco intoxication on erythrocyte deformability and possible correlation with hemoglobin–oxygen affinity and carboxyhemoglobin levels.
Methods or Approach:
In humans, the influence of smoking five cigarettes in 4 hours on carboxyhemoglobin levels, oxyhemoglobin dissociation cure, and erythrocyte deformability was investigated. Erythrocytes were incubated with different concentrations of carbon monoxide, monitoring carboxyhemoglobin levels, oxyhemoglobin dissociation curve, and red cell deformability.
Results to Date:
Effects of smoking five cigarettes included increased percentage of carboxyhemoglobin, reduced red cell deformability, and increased hemoglobin–oxygen affinity. Results suggest that the increase of carboxyhemoglobin percentage and the leftward shift of the oxyhemoglobin dissociation curve might cause chemical changes in hemoglobin structure and attendant abnormalities of internal red cell viscosity that could be responsible for the reduction in erythrocyte deformability.
Future Plans:
In vitro studies on the influence of carboxyhemoglobin levels on red cell deformability will be conducted.
Project Dates:
January 1982–January 1986.
Financial Support:
I.N.I.C. (MbL2).

0440. FACULTY OF MEDICINE OF LISBON, Department of Biochemistry, Avenue Egas Moniz, 1600 Lisbon, Portugal.

Project Title:
Exposure to Carbon Monoxide - Closed Areas and Professional Factors.

Principal Investigator:
Freitas, J.P.
Objective:
To study the influence of tobacco smoke as a major cause of exposure to carbon monoxide in enclosed public areas of Lisbon; examine workplace exposure to carbon monoxide.
Methods or Approach:
Carbon monoxide concentration in enclosed areas will be continuously recorded. Carboxyhemoglobin levels and oxyhemoglobin dissociation curve will be measured before and after occupational or nonoccupational exposure to carbon monoxide. Areas to be tested include a factory, a hospital, one public department, one train, and some pubs. Groups to be tested include taxidrivers, firemen, mechanics, medical doctors, and medical students.
Results to Date:
Among 55 metallurgists studied after working several hours in the factory, a significant increase of carboxyhemoglobin was found even in nonsmokers ($p<0.001$). In this group, the occupational environment appears to be an important factor in carbon monoxide poisoning.
Project Dates:
January 1982–January 1986.
Financial Support:
I.N.I.C. (MbL2).

REPUBLIC OF KOREA

0441. KOREA GINSENG AND TOBACCO RESEARCH INSTITUTE, 302 Shinseong-Dong, Joong-Gu, Daejeon-Shi, Choongcheongnam-Do, Republic of Korea.

Project Title:
Correlation Between Ornithine Decarboxylase as Polyamine Synthesis Enzyme and AHH Induced From Rats by Injection of Polycyclic Aromatic Hydrocarbon Compounds in Cigarette Smoke.

Principal Investigators:
Lee, Y.H.; Park, K.H.
Objective:
To elucidate induction of aryl hydrocarbon hydroxylase (AHH) and ornithine decarboxylase (ODC) by polycyclic aromatic hydrocarbons (PAH) and model polyamines action mode in cell culture.
Methods or Approach:
ODC activity is measured as release of $^{14}CO_2$ from DL-(1-^{14}C) ornithine, using a modification of the method of Beaven, Wilcox, and Terpsta. AHH is assayed and specific activity expressed in nmoles 3-OH-benzo(*l*)pyrene formed per mg protein/min.
Results to Date:
Project is in a preliminary phase.
Future Plans:
The in vitro experiment will be expanded to various tissues of several species and to cell cultures. Function of polyamines in cells will be studied and the dissociation between ODC and AHH induction in cell cultures treated with PAH compounds will be investigated utilizing inhibitors of ODC.
Project Dates:
January 1985–December 1987.
Financial Support:
Korea Ginseng and Tobacco Research Institute (K85TP-031).

0442. KOREA TOBACCO RESEARCH INSTITUTE, SMOKING AND HEALTH DIVISION, 302 Shinseong-Dong, Joong-Gu, Daejeon City, Choongnam, Republic of Korea.

Project Title:
Short Term Thermal Treatment System for Expanding Tobacco.

Principal Investigators:
Kim, K.H.; Lee, T.-H.; Yoo, K.-K., et al.
Objective:
To (1) develop and manufacture a less harmful cigarette; (2) reduce formation of harmful compounds in cigarette smoke; and (3) enhance usability of tobacco stems.
Methods or Approach:
Tobacco stems are expanded by superheated steam in a U-shaped, tubular expansion device that is provided with a Venturi tube and cooling jacket. Superheated steam, under high pressure, is ejected toward the Venturi tube. The rapid speed of the steam stream creates a Bernoulli flow (strong suction force in Venturi tube). Tobacco stems that are being continuously supplied into a hopper are thus automatically sucked into the expansion device via the Venturi tube. Stems are further puffed in a cyclone system.
Results to Date:
The short-term thermal treatment system improves quality by increasing filling power and combustibility, thus reducing tar and nicotine levels in smoke. The system also reduces amount of chlorinal contained in tobacco stems. When 10 percent of the filler is expanded by the system and used in a blend, tobacco weight reduction will be from 5 to 8 percent in some cases.
Future Plans:
Mechanisms by which harmful compounds are formed will be investigated.
Project Dates:
January 1980–December 1985.
Financial Support:
Office of Monopoly, Republic of Korea.

0443. KOREA TOBACCO RESEARCH INSTITUTE, BIOCHEMISTRY LABORATORY, 302 Shinseong-Dong, Joong-Gu, Daejeon-Shi, Choongcheongham-Do, Republic of Korea.

Project Title:
Variations of the Content and Isozyme Patterns of Cytochrome P-450 Complex From Rats by Injection of Polycyclic Aromatic Hydrocarbons of Cigarette Smoke.

Principal Investigators:
Mun, J.Y.; Park, K.H.
Objective:
To investigate content variation and activity of cytochrome P-450 complex when polycyclic aromatic hydrocarbons (PAH) of cigarette smoke are administered to rat liver; observe effects of saponin on recovery to normal condition.
Methods or Approach:
After treatment with PAH compounds (in vitro and in vivo) in rats, variations of cytochrome P-450 content were observed with spectrophotometry and isozyme pattern from rat liver microsomes was investigated using electrophoresis. Effects of the compounds on aryl hydrocarbon hydroxylases (AHH) activities, and changes in cytochrome P-450 isozyme patterns and cytochrome content were examined.
Results to Date:
Project is in a preliminary phase.
Future Plans:
Using antibody treatment, the composition ratio of cytochrome P-450 isozymes and isozyme patterns will be investigated; after treatment with ginseng extracts (ginseng saponin, ginsenoside), correlations between cytochrome P-450 isozymes and cytochrome b_5 will be studied. After separation of cytochrome P-450 isozymes, inhibitory effects of cigarette smoke in rat liver will be studied both in vitro and in vivo.
Project Dates:
January 1985–December 1987.
Financial Support:
Korea Ginseng and Tobacco Research Institute (K85TP-031).

ROMANIA

0444. LABOUR PROTECTION AND HYGIENE CENTRE, LABORATORY OF CYTOLOGY, Ministry of Chemical Industry, 59 Pop de Basesti, 73244 Bucharest, Romania. INSTITUTE OF HYGIENE AND PUBLIC HEALTH, Department of Occupational Medicine, 1-3 Dr. Leonte Street, 76256 Bucharest, Romania.

Project Title:
Role of Cigarette Smoking in Industrial Exposure to Soot and BCME.

Principal Investigators:
Herivan, R.; Constantinescu, V.; Melinte, L.
Objective:
To correlate effect of cigarette smoking in promoting pulmonary carcinoma with sputum cytological screening in workers exposed to soot and BCME.
Methods or Approach:
Sputum of exposed workers was collected for three consecutive mornings, fixed, and stained for cytology. Among the 244 soot-exposed workers, 87 were heavy smokers, 68 were light and occasional smokers, and 89 were nonsmokers. (Light and occasional smokers were included with nonsmokers in analyses). Median age was about 40 years, and average length of exposure was about 10 years. Of the 40 BCME-exposed workers, 19 were heavy smokers, 2 were light smokers, and 19 were nonsmokers. Average age was about 33.6 years; average exposure was 4.2 years. Cytological findings for exposure to soot and BCME were compared with findings for 200 controls (over 40 years of age, smokers and nonsmokers). Results are reported by an adaptation of Papanicolaou's classification.
Results to Date:
Marked atypia were found only in workers chemically exposed to BCME; 4.8 percent of smokers and 6.2 percent of nonsmokers. The biological mechanism for increased injury in nonsmokers from short-term exposure to BCME has not yet been determined. More smokers than nonsmokers showed moderate atypia; 38.5 percent and 14.5 percent, respectively. Moderate atypia was also seen in soot-exposed workers (10.5 percent of smokers and 4.2 percent of nonsmokers), and in control group smokers (9.7 percent). Mild atypia was found in both smokers and nonsmokers in all groups: (1) soot-exposed, 34.2 percent

smokers and 11.8 percent nonsmokers; (2) BCME-exposed, 52.3 percent and 31.2 percent, respectively; and (3) controls, 32.0 percent and 14.9 percent, respectively.

Project Dates:
April 1983–December 1986.

Financial Support:
Ministry of Chemical Industry, Romania; Institute of Hygiene and Public Health, Romania.

SOUTH AFRICA

0445. MEDICAL RESEARCH COUNCIL, NATIONAL RESEARCH INSTITUTE FOR NUTRITIONAL DISEASES, P.O. Box 70, Tygerberg 7505, South Africa.

Project Title:
Smoking and Esophageal Cancer.

Principal Investigators:
Van Rensburg, S.J.; Rose, E.F.

Objective:
To assess the role of tobacco in the etiology of esophageal cancer in Africans.

Methods or Approach:
Tobacco-derived materials have been subjected to Ames mutagenicity testing and to in vivo tests on rats. Case-control questionnaire studies have been conducted.

Results to Date:
Home-grown Transkeian tobacco yields condensates that are more mutagenic than any other known comparable substance. The condensate and ash in pipes are often consumed. Experimentally they induce some esophageal pathology. The case-control study indicates the relative importance of various tobacco-related habits.

Project Dates:
March 1975–1983.

Financial Support:
MRC, South Africa; National Cancer Association of South Africa.

0446. RESEARCH GROUP IN DENTAL EPIDEMIOLOGY, Department of Oral Pathology, Private Bag XI, Tygerberg, 7505 South Africa.

Project Title:
Submucous Fibrosis: An Epidemiologic Study.

Principal Investigators:
Seedat, H.A.; Van Wyk, C.W.

Objective:
To determine prevalence of betel nut chewing, submucous fibrosis, and oral cancer among South African Indians; study relationship between submucous fibrosis, betel chewing, intake of spicy foods, smoking, and alcohol consumption.

Methods or Approach:
A random sample of households was selected and a questionnaire was completed for each household member. Cases with signs of submucous fibrosis were referred for biopsies and histological features were evaluated. In addition, all cases of submucous fibrosis that had been referred to the hospital were histologically investigated.

Results to Date:
Betel chewers constituted 9 percent of the study population and 38 percent of chewers had features of submucous fibrosis; 5 percent of submucous fibrosis cases had oral squamous carcinomas. A significant relationship existed between betel chewing and submucous fibrosis, but not with intake of spicy foods, smoking, or alcohol consumption.

Project Dates:
1981–1985.

Financial Support:
MRC, South Africa.

0447. UNIVERSITY OF CAPE TOWN MEDICAL SCHOOL, Department of Community Health, Cape Town 7925, South Africa.

Project Title:
Smoking Habits of Nurses.

Principal Investigators:
Disler, P.B.; Jacka, E.; Sayed, A.R., et al.

Objective:
To evaluate smoking habits of nurses; compare habits of nurses working in community health positions with those of nurses working within institutions.

Methods or Approach:
A questionnaire on smoking habits was sent to all nurses working in community health and in institutions. Information was collected on age, sex, civil status, and educational background; status in nursing; current and previous smoking behavior; attitudes toward allowing smoking in public transport, cinemas, restaurants, and supermarkets; and opinions about the value of not smoking as a prophylactic measure against lung cancer (to assess knowledge of the harmful effects of smoking).

Results to Date:
In both groups, > 80 percent thought that smoking should not be allowed in public transport, cinemas, and supermarkets, and approximately 70 percent thought that it should be banned in restaurants. However, many nurses were unclear about the importance of not smoking in prevention of lung cancer. Nurses working in the community smoked less than those in institutions (who were also younger, better educated, and constituted a greater proportion of registered nurses). The major difference was in the proportion that had never smoked (45.2 percent of institutional nurses vs. 59.5 percent of community nurses). It may be that a difference in personality led nurses to choose a career in community health and also to decide not to smoke. Smoking prevalence was comparable with that reported from other countries (22.8 percent of community vs. 37.6 percent of institutional nurses).

Project Dates:
January 1982–July 1982.

Financial Support:
University of Cape Town Research Fund.

Reference:
Jacka, E.; Disler, P.B.; Sayed, A.R., et al. "Smoking Habits of Nurses." *Curationis*, pp. 37-39, March 1984.

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SUDAN

0448. MINISTRY OF HEALTH AND AHFAD COLLEGE FOR WOMEN, P.O. Box 8025, Al-Amarat, Khartoum, Sudan.

Project Title:
Epidemiological Survey of Smoking Among Sudanese Doctors.

Principal Investigator:
Arabi, M.A.

Objective:
To (1) define incidence of smoking among a randomized sample of doctors; (2) determine how smoking habit started and factors that influenced initiation; (3) determine attitudes toward smoking as a health hazard; (4) establish whether doctors believe in cessation and the percentage that have tried to quit; and (5) compare incidence of hypertension, ischemic heart disease, peptic ulcer, and bronchitis among smokers and nonsmokers.

Methods or Approach:
Questionnaires, based on WHO questionnaire guidelines for group surveys, were used to interview a representative sample of approximately 500 Sudanese doctors. The sample is randomized and statistically significant.

Results to Date:
Data indicate that (1) two-thirds of Sudanese doctors are smokers; (2) 80 percent have smoked for more than 5 years; (3) most smokers consume from 10 to 20 cigarettes/day; (4) 90 percent of smokers are aware of the health hazards; and (5) 70 percent have tried to quit but failed. Factors in smoking initiation included peer groups (40 percent), followed by parents, relatives, and propaganda. Teachers were not an influencing factor in initiation or maintenance of smoking. Significantly more smokers suffer from smoking-related diseases compared with nonsmokers.

Future Plans:
A similar pilot study will be conducted among adolescent schoolchildren 3 years before entering the university, and among university and higher school students to examine epidemiologic, demographic, and psychological factors identified with smoking initiation or establishment of the smoking habit. A pilot study will also be conducted among women in Khartoum.

Project Dates:
June 1984–June 1986.

Financial Support:
Sudan Anti-Smoking Society and Ahfad College for Women. Sudan.

SWEDEN

0449. HUDDINGE UNIVERSITY HOSPITAL, Department of Obstetrics and Gynecology, S-141 86 Huddinge, Sweden.

Project Title:
Acute Metabolic and Circulatory Effects of Cigarette Smoking in Late Pregnancy.

Principal Investigators:
Nylund, L.; Lunell, N.-O.; Persson, B., et al.

Objective:
To study the acute effects of smoking in pregnancy; make comparisons between different groups of high-risk pregnancies with regard to these effects.

Methods or Approach:
Women in the last trimester of pregnancy were asked to participate in the study. All were habitual smokers. Some patients had a normal pregnancy, but women with diabetes mellitus, preeclampsia, and intrauterine growth retardation also took part. The patients were in the supine position. Blood samples were obtained from a forearm vein. Fetal heart rate was recorded continuously with ultrasound cardiotachography. Maternal heart rate and blood pressure were measured at intervals. After a resting period, the subjects were asked to smoke two cigarettes, inhaling as usual. Blood samples were drawn before and after the smoking period.

Results to Date:
There was a striking cardiovascular response to smoking. Both maternal and fetal heart rate rose significantly and the systolic and diastolic maternal blood pressure responded in the same way. Plasma glucose, plasma 3-hydroxybutyrate, and nonesterified fatty acids increased. Cyclic AMP also showed a significant rise which could indicate a catecholamine-mediated effect. Recent results indicate that diabetic women are more sensitive to the glucose-elevating effect of smoking than their normal controls. Also 3-hydroxybutyrate seems to rise to higher values in diabetic women.

Future Plans:
Work is in progress to identify what groups of pregnant women are most sensitive to the circulatory and metabolic effects of cigarette smoking.

Project Dates:
June 1978–continuing.

Financial Support:
Allmanna BB:s Minnesfond; First of May Flower Annual Campaign for Children's Health.

0450. HUDDINGE UNIVERSITY HOSPITAL, Department of Obstetrics and Gynecology, S-141 86 Huddinge, Stockholm, Sweden.

Project Title:
Influence of Cigarette Smoking on the Fibrinolytic Activity of the Vein Wall in Healthy Women and Pill Users.

Principal Investigators:
Kyaeldgaard, A.; Larsson, B.

Objective:
To investigate influence of cigarette smoking and treatment with oral contraceptives (OC), separately and in combination, on fibrinolytic activity of vein walls (FAV) in healthy women of childbearing age.

Methods or Approach:
In healthy women (aged 16 to 46 years) without predisposing factors for thromboembolic diseases, FAV is determined using a semiquantitative fibrin slide technique. Data on age, menstrual cycle, smoking habits, and use of OCs (including type and duration of use) are registered prior to sampling and used

for distribution of material into subgroups consisting of young and middle-aged (≥35 years), nonsmoking and smoking controls or pill users.

Results to Date:
Preliminary results show a significant decrease in FAV in the three middle-aged subgroups (smokers, smoking pill users, and nonsmoking pill users who had used OCs continuously for about 10 years). No such effect was found in corresponding younger groups.

Project Dates:
1978–continuing.

Financial Support:
Swedish Tobacco Company (83-17).

0451. HUDDINGE UNIVERSITY HOSPITAL, Department of Obstetrics and Gynecology, S-141 86 Huddinge, Stockholm, Sweden.

Project Title:
Influence of Smoking and Contraceptive Hormones on the Fibrinolysis in Rats.

Principal Investigators:
Kjaeldgaard, A.; Larsson, B.

Objective:
To investigate effect of cigarette smoke exposure on fibrinolysis in rats with and without concomitant treatment with a combination of the two most commonly used contraceptive steroids, ethinylestradiol (EE_2) and levonorgestrel (Ng).

Methods or Approach:
Female rats (200 g) were divided into four groups (10 each). Two groups were treated with EE_2 + Ng in daily subcutaneous sesame oil injections. One treated and one untreated group were exposed to smoke of 10 cigarettes twice/day for 6 weeks in a complete chamber exposure system with a capacity of six cigarettes/hour. Fibrinolytic activity in plasma (FAP) and in vessel wall (FAV) was determined using fibrin plate and histochemical fibrin slide techniques, respectively.

Results to Date:
Carbon monoxide determinations immediately after exposure to 3 and 10 cigarettes corresponded well with previous results obtained in humans. In smoke-exposed rats, a significant decrease in FAV was recorded and a significantly negative correlation between FAV and FAP was demonstrated. FAV decrease was more pronounced in hormone-treated rats exposed to cigarette smoke. However, no effect of the treatment with the combination of the two contraceptive hormones was demonstrated. Results suggest that impaired vascular fibrinolysis associated with cigarette smoking may be caused by increased release of plasminogen activators (situated in the vessel wall) to the blood stream.

Future Plans:
Additional investigations with higher treatment doses of the two contraceptive hormones are in progress.

Project Dates:
June 1982–1985.

Financial Support:
Swedish Tobacco Company (82-27; 83-17).

0452. HUDDINGE UNIVERSITY HOSPITAL, Department of Clinical Physiology, S-141 86 Huddinge, Sweden.

Project Title:
Role of Cardiovascular Prostanoids in Health, During Smoking, and in Cardiovascular Disease.

Principal Investigator:
Wennmalm, A.

Objective:
To study the role of prostaglandin I_2 (PGI_2) and of thromboxane in cardiovascular function in health and disease; investigate how smoking interferes with these roles.

Methods or Approach:
Tissue homogenates or subcellular fractions of various cardiovascular tissues are incubated with prostaglandin precursors with and without various concentrations of nicotine, and resulting formation of PGI_2 is determined. In other experiments, intact organs are perfused with salt solution with or without nicotine, and basal and stimulated efflux of PGI_2 is analyzed. Rats are exposed to cigarette smoke in acute and chronic experiments, and organ synthesis of PGI_2 and thromboxane (in platelets) is assessed. Urinary excretion of thromboxane and PGI_2 metabolites are assessed in smokers and nonsmokers.

Results to Date:
Nicotine interferes with cardiovascular formation of PGI_2 by inhibiting cyclo-oxygenase (the enzyme that converts arachidonic acid to prostaglandin endoperoxide). Similar activity does not take place in platelets, implying that nicotine impairs PGI_2 but not thromboxane formation in the cardiovascular system. Such an effect may disturb platelet function in a proaggregatory direction and thereby provide a basis for increased thrombogenic activity following nicotine exposure during cigarette smoking.

Future Plans:
Research will investigate the effect of cigarette smoking on thromboxane and PGI_2 formation in smokers and nonsmokers to determine whether the effect of nicotine observed in isolated tissues and organs can be extrapolated to human subjects.

Financial Support:
Huddinge University Hospital; MRC, Sweden; Council for Tobacco Research, U.S.A., Inc.

0453. KAROLINSKA HOSPITAL, Department of Occupational Medicine, Box 60500, S-104 01 Stockholm, Sweden.

Project Title:
Lung Cancer, Residency and Smoking.

Principal Investigators:
Axelson, O.; Edling, C.; Kling, H.

Objective:
To further evaluate earlier findings by investigating lung cancer on Oeland, a Baltic island, with a rural population and only three small towns of about 2,000 inhabitants.

Methods or Approach:
A case–referent approach is utilized. The study period was from 1960 to 1978 and the cases are those who had died of lung cancer and a random sample of controls. Exposures, dwellings where cases of referents had lived, are categorized according to building material and location. Measurements of radon daughters on alpha-sensitive film are made in the houses, and smoking habits are obtained by interviews with next of kin.

Results to Date:
During the study period, in a population of about 20,000, 61 lung cancer deaths were recorded. A preliminary calculation based on 29 cases and 208 controls who had lived in the same house for 30 years or more before death showed a higher risk for lung cancer among those who had lived in stone houses on radiation ground. Data also seem to indicate the possibility of a multiplicative effect between smoking and exposure to radon

and radon daughters in homes, but there was also some confounding between these factors in the data.

Project Dates:
September 1979–1983.

Financial Support:
Swedish Governmental Committee on Radon in Homes.

References:
(1) Axelson, O.; Sundell, L.; Edling, C. "Mining, Smoking and Lung Cancer." *Scandinavian Journal of Work, Environment and Health* 5: 10-15, 1979. (2) Edling C.; Kling, H.; Axelson, O. "Radon in Homes – A Possible Cause of Lung Cancer." *Scandinavian Journal of Work, Environment and Health* 10:25-43, 1984.

0454. KAROLINSKA INSTITUTE, Department of Histology and Research and Development Laboratory, Department of Obstetrics and Gynaecology, Box 60400, S-104 01 Stockholm, Sweden.

Project Title:
Smoking, Catecholamines, Neuropeptides and Neuroendocrine Functions.

Principal Investigators:
Fuxe, K.; Andersson, K.; Eneroth, P., et al.

Objective:
To map out endocrine disturbances induced by nicotine and smoking in male and female rats with different endocrine states.

Methods or Approach:
Research will focus on alterations in pituitary hormone secretion and how disturbances can be brought about by actions on the neurochemistry in the hypothalamus and the preoptic area. Serum hormone levels are determined by radioimmunoassay, and neurochemistry of the hypothalamus and preoptic region is evaluated by biochemical, histochemical, morphometrical, and microdensitometrical procedures, focusing on measurements of catecholamines and various types of neuropeptides and their receptors. Methods are used to analyze actions of nicotine and smoking on pre- and postsynaptic features of monoamine and neuropeptide neurons in the hypothalamus and the preoptic region and to relate changes to disturbances in endocrine function.

Results to Date:
Acute intermittent exposure to cigarette smoke induces reductions in dopamine (DA) and noradrenaline (NA) levels, and a dose-dependent reduction of TSH, prolactin, and LH serum concentrations. Effects can be related to nicotine in cigarette smoke, since exposure to filtered smoke or to mecamylamine pretreatment of rats exposed to unfiltered smoke completely blocks all effects mentioned. Chronic exposure to cigarette smoke induced a tolerance in certain hypothalamic catecholamine neuronal systems, and also induced a tolerance to cigarette smoke-induced enhancement of corticosterone levels in serum.

Future Plans:
Models that may mimic the medico-social situation in man where neuroendocrine disturbances may be caused by smoking are being sought. Specifically, aims are to (1) further characterize effects of nicotine and smoking on neuroendocrine function in normal male rats; (2) determine if previous neuroendocrine results in male rats can be obtained in female rats; (3) characterize the interaction between smoking and neuroendocrine function; and (4) characterize neuroendocrine disturbances produced by acute and chronic exposure to cigarette smoke in spontaneously hypertensive rats.

Project Dates:
January 1983–continuing.

Financial Support:
CTR.

0455. KAROLINSKA INSTITUTE, FACULTY OF ODONTOLOGY, Department of Periodontology, Stockholm, S-141 04 Huddinge, Sweden.

Project Title:
Suppression of Inflammatory Vascular Reaction in the Gingiva of Smokers.

Principal Investigators:
Bergstrom, J.; Preber, H.

Objective:
To produce experimental gingivitis in humans; study vascular reaction associated with developing gingival inflammation in smokers and nonsmokers.

Methods or Approach:
Gingivitis is produced by abstention from oral hygiene for 30 days. Vascular reaction of marginal gingiva adjacent to teeth in the lower anterior region is studied by (1) bleeding proneness as determined from electronic pressure probing; (2) exudation measured quantitatively on filter strips; and (3) vascular topography as documented by clinical closeup stereophotography.

Results to Date:
In a series based on 10 smokers and 10 nonsmokers (aged 18 to 30 years and with healthy periodontia) the parameters were studied over time. Results indicate that although increasing with time in both groups, bleeding and exudation parameters were significantly less elevated in smokers. Preliminary data on vascular events support the findings. To date, findings indicate suppression of gingival vascular response to the challenge of plaque accumulation over a 30-day period.

Future Plans:
Since more detailed information seems to be warranted, plans are in progress to extend studies into the field of animal experimentation.

Project Dates:
June 1984–May 1986.

Financial Support:
Karolinska Institute, Sweden.

0456. KAROLINSKA INSTITUTE, Department of Pedodontics, Odontological Clinics, Box 4064, S-141 04 Huddinge, Sweden.

Project Title:
Relation Between Tobacco Consumption and Oral Health in Swedish Schoolchildren.

Principal Investigators:
Modeer, T.; Lavstedt, S.; Ahlund, C.

Objective:
To study the relationship between use of tobacco and oral health in schoolchildren.

Methods or Approach:
Participants were 232 school children (119 boys and 113 girls, mean age 13.5 years) from Huddinge, on the outskirts of Stockholm. All children received dental treatment at the same public dental clinic. Socioeconomic status was 7 percent upper, 54 percent middle, and 36 percent lower or working class (social class unknown for 3 percent). Prior to clinical examination, children answered questions about smoking, snuff-dipping, and toothbrushing habits. Oral hygiene was registered according to the Plaque Index (PII) of Silness and Loe, and

degree of gingival inflammation was estimated on the basis of the Gingival Index (GI) of Loe and Silness.

Results to Date:
Tobacco was used regularly by 21.5 percent of the children (69 percent girls and 31 percent boys). Mean number of cigarettes smoked/day was 5.3 for girls and 4.6 for boys. Heavy smokers among boys (>10 cigarettes/day) had significantly ($p<0.05$) higher values of GI and PII than nonsmokers, but this was not applicable to girls. Smoking expressed as "number of cigarettes" was a significant indicator for PII, decayed surfaces, and filled spaces. Although none of the girls took snuff regularly, 11 percent of the boys did (mean consumption five pinches/day). Snuff was present in the oral cavity for an average of 3.5 hours. Snuff-dipping showed a strong significant correlation ($p<0.001$) with GI after controlling for PII.

Financial Support:
Karolinska Institute, Sweden.

0457. LINKOPING UNIVERSITY, UNIVERSITY HOSPITAL, Departments of Otolaryngology, Oncology, and Pathology, S-581 85 Linkoping, Sweden.

Project Title:
Dysplasia and Carcinoma of the Upper Respiratory Tract.

Principal Investigators:
Olofsson, J.; Lundgren, J.; Klintenberg, C., et al.

Objective:
To review all patients treated for nasal and paranasal sinus carcinoma and laryngeal dysplasia and carcinoma at Linkoping University Hospital during the last two decades.

Methods or Approach:
The review is retrospective and prospective, based on a questionnaire used since the early 1970s. Smoking habits and occupational exposures will be considered. The role of continued smoking following initial treatment for laryngeal dysplasia or carcinoma will be evaluated in relation to rate of recurrence and progress of the disease.

Results to Date:
Results are not yet available.

Financial Support:
Ostergotlands Lans Landsting, Sweden.

0458. LUND UNIVERSITY HEALTH SCIENCES CENTER, S-240 10 Dalby, Sweden.

Project Title:
Influence of Smoking on Thyroid Hormone Economy and Goiter Formation.

Principal Investigator:
Melander, A.

Objective:
To assess if and how smoking smoking influences the production, secretion, and turnover of thyroid hormones in man, including effects on thyroidal uptake of iodide, secretion of thyroglobulin, and formation of goiter.

Methods or Approach:
Radioimmunoassays of iodothyronines and of thyroglobulin are performed.

Results to Date:
The data accumulated so far strongly suggest that smoking has at least two, calorigenically opposed, effects on thyroid hormone economy. Smoking may enhance the secretion of thyroid hormone and/or increase the extrathyroidal formation of T_3 from T_4 at the expense of rT_3 formation. This effect may be subsequent to an enhanced sympathetic activity. In addition, smoking may have a goitrogenic effect, possibly via the presence of thiocyanate in the smoke, expressed as direct observation of an increased goiter frequency in smoking women, together with increased levels of circulating thyroglobulin.

Future Plans:
Preliminary data will be verified.

Project Dates:
1977–continuing.

Financial Support:
MRC, Sweden (3880); Swedish Tobacco Company.

0459. NATIONAL INSTITUTE OF ENVIRONMENTAL MEDICINE, Box 60208, 104 01 Stockholm, Sweden.

Project Title:
Passive Smoking and Lung Cancer.

Principal Investigators:
Pershagen, G.; Hrubec, Z.; Svensson, C.

Objective:
To study the risk of lung cancer among nonsmoking women in relation to smoking habits of family members, especially the husband.

Methods or Approach:
Subjects are nonsmoking women in a sample of the Swedish population for whom smoking habits were investigated in 1963 and nonsmoking women in the Swedish twin registry (smoking data obtained in 1961, 1967, and 1970). Cause-specific mortality for the 26,000 women will be updated through 1980. Controls will be selected from the cohort for women with lung cancer. A next of kin to each study subject will be interviewed about smoking habits of family members, occupations of the women, and other factors.

Results to Date:
In an update of mortality, it was found that 49 nonsmoking women in the 1963 sample and 26 nonsmokers in the twin registry had lung cancer. It is expected that the total number of female lung cancer cases will be around 80.

Project Dates:
July 1982–June 1985.

Financial Support:
Swedish Cancer Society (1878-B83-OIX).

0460. REGIONAL HOSPITAL, Department of Occupational Medicine, S-701 85 Orebro, Sweden.

Project Title:
Symptoms of Bronchitis–Validation of a Questionnaire.

Principal Investigators:
Ohlson, C.-G.; Hogstedt, C.

Objective:
To investigate the reliability and validity of two questionnaires about respiratory symptoms; construct a screening instrument for chronic bronchitis.

Methods or Approach:
Two self-administered questionnaires were sent to 410 asbestos cement exposed workers and to 100 unexposed controls. One of the questionnaires is a Swedish translation of the MRC questionnaire about symptoms of bronchitis. Reliability was tested by comparing the answers on the same questionnaires sent to a subsample with a time interval of 3 weeks. The answers were validated against clinical diagnoses, smoking history, lung function tests, and x-ray examinations.

Results to Date:
The reproducibility of the questions seems to be very good for some questions and acceptable for others. Answers correspond well with the histories obtained by a physician. Particularly,

the MRC questionnaire seems to discriminate on a group basis between chronic bronchitis and health. Neither the MRC nor the Swedish questionnaire was sufficiently valid for screening purposes for chronic bronchitis. The sensitivity of the questionnaires for detecting chronic bronchitis was around 65 percent with the use of three or more yes answers as screening criteria. Specificity was around 75 percent, indicating that the number of false positives may be inconveniently high. The classical definition of chronic bronchitis with emphasis on mucus hypersecretion is questioned by these results; however, with these drawbacks in mind, both questionnaires can be recommended for screening purposes.

Project Dates:
September 1980–1982.

Financial Support:
County Councils; Swedish Work Environment Fund.

Reference:
Ohlson, C.-G.; Hogstedt, C. "Symptoms of Bronchitis–Validation of a Questionnaire." *Arbete och Halsa* 27, 1984.

0461. REGIONAL HOSPITAL, Departments of Periodontology and Oral Pathology, S-631 88 Eskilstuna, Sweden.

Project Title:
The Ultrastructure of the Gingival Epithelium in Smokers' Melanosis.

Principal Investigators:
Hedin, C.A.; Larsson, A.

Objective:
To study ultrastructure of melanocytes and keratinocytes in attached gingiva from clinically pigmented and nonpigmented tissue from smokers and nonsmokers with light and electron microscopy; correlate clinically observed melanin pigmentation to histological findings and to smoking.

Methods or Approach:
Tissue was taken within attached gingiva in pigmented and nonpigmented regions in smokers and nonsmokers (15 patients, aged 15 to 50 years). Gingival inflammation was low. Tissue was immediately prepared for light and electron microscopy. Smoking habits were determined.

Results to Date:
Clinically observed pigmentation consisted of melanin. Histologic appearance in pigmented tissue from smokers and nonsmokers did not differ. In clinically nonpigmented tissue from molar regions in smokers, a higher number of keratinocytes were found to contain melanin compared with clinically nonpigmented tissue from nonsmokers. In nonpigmented nonsmokers, melanosomes in melanocytes had a very low state of maturation, with little melanin. Few keratinocytes contained melanosomes. Tobacco smoking was correlated to pigmentation, but other factors could also cause oral melanin pigmentation. Smoking did activate melanocytes and keratinocytes in a nonspecific way. Melanin may have a role as binder of toxic products, such as free radicals or polycyclic compounds, and thus protect cells from damage while transporting agents through the epithelium.

Future Plans:
The cross-cut diameter of compound melanosomes in keratinocytes will be studied further. Large melanosome compounds, containing more than 100 melanosomes, were found for the first time in pigmented gingiva of smokers and nonsmokers.

Financial Support:
MRC, Sweden.

Reference:
Hedin, C.A.; Larsson, A. "The Ultrastructure of the Gingival Epithelium in Smokers' Melanosis." *Journal of Periodontal Research* 19(2):177-190, March 1984.

0462. SABBATSBERG HOSPITAL, Departments of Pathology and Cytology, Box 6401, S-113 82 Stockholm, Sweden.

Project Title:
Cytopathological, Cytochemical, and Prospective Studies of Bronchial Epithelial Abnormalities in Cigarette Smokers.

Principal Investigators:
Nasiell, M.; Roger, V.; Kinnman, J., et al.

Objective:
To (1) investigate the possiblilty of detecting early lung cancer by sputum cytology in asymptomatic high risk cigarette smokers; (2) establish cytomorphological criteria for early squamous cell carcinoma of the bronchi; (3) investigate natural history of atypical squamous metaplasia/dysplasia of the bronchi at cytologic long-term followup; (4) study biological significance of various degrees of atypical squamous metaplasia by quantitative analysis of DNA and total protein content in human and experimental material; and (6) determine if, and at which level of atypia, epithelial lesions are reversible.

Methods or Approach:
Subjects are chest clinic patients and a screening series of asymptomatic high-risk smokers (men >45 years of age who smoke ≥ 20 cigarettes/day). Sputa are obtained at home and delivered to the laboratory by mail. Cytomorphologic grading of atypical metaplasia, early bronchial malignancy, and advanced lung cancer is determined on Papanicolaou-stained sputum preparations (12 slides). Asymptomatic x-ray negative patients with more pronounced (moderate-severe) atypia of metaplastic cells are examined twice/year on a long-term basis. After destaining and subsequent Feulgen-staining, nuclear amount of DNA and total protein in atypical metaplastic cells are measured in a cytospectrophotometer.

Results to Date:
As of January 1985, 28 lung cancers have been found in 3,042 (0.9 percent) asymptomatic smokers. In 23 patients, cytologic findings were compatible with early squamous cell carcinoma; 12 patients have been resected with 5-year survival of 50 percent (6 patients). Atypical metaplasia (mild-moderate) was found in 7.9 percent, and severe atypia in 0.7 percent. Among chest clinic patients with positive sputum cytology (squamous cell carcinoma), some were clinically occult initially (x ray negative) and 12 have been resected for early squamous cell cancer. The 5-year survival rate was 42 percent (5 patients). There are also indications that in certain patients, severe squamous metaplastic cell atypia or cancer in situ may be reversible when the smoker reduces or stops smoking. Results are in agreement with dog experiments that indicated regression of advanced atypia/cancer in situ when injections of the carcinogen were stopped. Results achieved by quantitative cytochemical analysis of metaplastic and dysplastic cells in human clinical sputum material and in the experimental dog series indicate an association between increasing cellular atypia and increasing degree of heteroploidy, suggesting a significant progressive epithelial process during development of squamous cell lung cancer.

Future Plans:
Patients with atypical squamous metaplasia are followed for continued study of lung cancer pathogenesis. Dog experiments, including production of bronchogenic carcinoma by repeated injections of methylcholanthrene, are continued for further pathogenetic studies, and to determine whether or not certain lesions are reversible when exposure is stopped. A study with

the same purpose in humans with advanced bronchoepithelial atypias is under way.
Project Dates:
1964–continuing.
Financial Support:
Swedish Tobacco Company; Swedish Cancer Society; Tokyo Medical College.

0463. SAHLGRENSKA HOSPITAL, Medical Department I, S-413 45 Gothenburg, Sweden.

Project Title:
Obesity Following Tobacco Withdrawal.

Principal Investigator:
Bjorntorp, P.
Objective:
To determine why withdrawal of tobacco is followed by increase in body weight; establish whether smoking is an arrhythmia-inducing factor.
Methods or Approach:
The current investigation comprises analyses of weight gain and arrhythmia incidence, before and after 14 days of abstention from smoking. Subjects were smokers with histories of myocardial infarction. Tendencies to experience arrhythmia after smoking will be studied during work tests with recordings of ventricular extrasystoles.
Results to Date:
Obesity resulting from tobacco withdrawal was not associated with reinfarction.
Project Dates:
1977–1984.
Financial Support:
Swedish Tobacco Company (7619).

0464. SAHLGRENSKA HOSPITAL, Medical Department II, S-413 45 Gothenburg, Sweden.

Project Title:
The Population Study of Women in Gothenburg, Sweden.

Principal Investigators:
Bengtsson, C.; Lapidus, L.; Hallstrom, T.
Objective:
To study the female population in Gothenburg from different points of view, including internal medicine, psychiatry, gynecology, surgery, nutrition, and odontology; determine what effect smoking has on health.
Methods or Approach:
A representative sample of the female population in Gothenburg, first studied in 1968-1969, and restudied in 1974-1975 and 1980-1981, includes women born in 1908, 1914, 1918, 1922, and 1930. In the first examination, 1,462 women participated. In the 12-year followup study (1980-1981), women aged 38 and 26 (born in 1942 and 1954, respectively) were also included. In addition to a physical examination, blood and urine tests, and electrocardiogram, questions were asked about smoking habits.
Results to Date:
Data from 1968 show that women who smoke begin menopause about 2 years earlier than nonsmokers. Longitudinal data show increased body weight in women who stopped smoking. Between 1968 and 1970, all women who had myocardial infarction (MI) in Gothenburg and who were of the same age as program participants were subjects of a special study. Smoking was much more common among women who had MI than in women of the same age in the population study. No such difference was observed between women with angina pectoris and other women. Women who smoked had slighty worse prognosis with respect to MI incidence and death during 12-year followup, but no significant differences were observed. Data analysis is continuing.
Project Dates:
1968–continuing.
Financial Support:
Sahlgrenska Hospital, Gothenburg; MRC, Sweden.

0465. SWEDISH FARMERS' SAFETY AND PREVENTIVE HEALTH ASSOCIATION, Lantbrukshalsan, 105 33 Stockholm, Sweden.

Project Title:
Respiratory Disorders in Farming Populations.

Principal Investigator:
Thelin, A.
Objective:
To study different farming populations to determine reasons for accumulation of lung diseases among farmers.
Methods or Approach:
To determine the relationship between farming and different forms of lung disorders, epidemiological techniques and environmental classification were used to evaluate reactions in farming populations.
Results to Date:
In the farming populations studied, there were no significant differences in reactions of smokers and nonsmokers. Bacterial endotoxins are connected to dust in swine confinement buildings and poultry houses. Different symptoms are reported by workers; workers in poultry confinement buildings had decreased forced expiratory volume in 1 sec. The most pronounced reactions were at sites where levels of dust and endotoxin were high.
Future Plans:
Studies will be continued with swine confinement workers.
Project Dates:
August 1983–1987.
Financial Support:
Swedish Farmers' Safety and Preventive Health Association.
Reference:
Thelin, A.; Tegler, O.; Rylander, R. "Lung Reactions During Poultry Handling Related to Dust and Bacterial Endotoxin Levels." *European Journal of Respiratory Disease* 65:266-271, 1984.

0466. SWEDISH NATIONAL FOOD ADMINISTRATION, Box 622, S-751 26 Uppsala, Sweden.

Project Title:
N-Nitrosamines in Snuff and Chewing Tobacco.

Principal Investigators:
Osterdahl, B.-G.; Slorach, S.A.
Objective:
To determine levels of volatile N-nitrosamines, tobacco-specific N-nitrosamines, and other nonvolatile N-nitrosamines (e.g., N-nitrosodiethanolamine) in snuff and chewing tobacco on the Swedish market.
Methods or Approach:
Snuff and chewing tobacco samples are purchased on the Swedish market and analyzed for N-nitrosamines using gas chromatography-thermal energy analysis. Effect of storage under various conditions on N-nitrosamine content in snuff is also examined.
Results to Date:
Detectable levels of N-nitrosodimethylamine and N-nitroso-

pyrrolidine were found in nearly all of the 90 samples (from 1981 to 1983) of snuff and chewing tobacco analyzed. N-nitrosopiperidine and N-nitrosomorpholine were also found in some samples. In most samples, total concentration of volatile N-nitrosamines was < 10 µg/kg; however, levels of tobacco-specific N-nitrosamines were much higher. All 36 snuff samples analyzed contained detectable levels of N'-nitrosonornicotine, N'-nitrosoanatabine, N'-nitrosoanabasine, and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone. Total concentration of tobacco-specific N-nitrosamines was between 2.5 and 51 mg/kg. Detectable levels (≤ 4.4 mg/kg each) of at least two of the four tobacco-specific N-nitrosamines were found in all 18 samples of chewing tobacco analyzed. Storage of snuff in unopened boxes for 20 to 30 weeks resulted in only small changes in levels; however, storage in boxes that had been opened and resealed resulted in a large increase in mean level of total volatile N-nitrosamines.

Future Plans:

Levels of N-nitrosodiethanolamine will be determined in snuff and chewing tobacco, and levels of tobacco-specific N-nitrosamines in saliva of snuff dippers will be determined.

Project Dates:

January 1981–December 1985.

Financial Support:

Swedish National Food Administration.

References:

(1) Osterdahl, B.-G.; Slorach, S.A. "Volatile N-Nitrosamines in Snuff and Chewing Tobacco on the Swedish Market." *Food and Chemical Toxicology* 21(6):759-762, December 1983. (2) Osterdahl, B.-G.; Slorach, S.A. "N-Nitrosamines in Snuff and Chewing Tobacco on the Swedish Market in in 1983." *Food Additives and Contaminants* (In press).

0467. THE NATIONAL INSTITUTE OF ENVIRONMENTAL MEDICINE, Department of Epidemiology, Box 60208, S-104 01 Stockholm, Sweden.

Project Title:

Case-Referent Study of Pancreas Cancer.

Principal Investigator:

Norell, S.E.

Objective:

To study the possible relationship between pancreatic cancer and previous chemical exposure and factors such as smoking and alcohol consumption.

Methods or Approach:

A case-referent study with two referent groups has been designed to assess the association between chemical exposure and pancreatic cancer. Histories of chemical exposure related to work, housing, diet, smoking, and other factors will be obtained from 100 incident cases of pancreatic cancer, 100 clinical controls from the same hospitals, and nonclinical controls from the area population.

Results to Date:

Data collection will be completed during 1984.

Project Dates:

1980–1985.

0468. ULLERAKER HOSPITAL, SMOKING CESSATION CLINIC, S-750 17 Uppsala, Sweden.

Project Title:

Effects of Number of Treatment Sessions and Nicotine Gum in Physician Based Smoking Cessation.

Principal Investigator:

Fagerstrom, K.-O.

Objective:

To investigate effectiveness of nicotine chewing gum in cessation of smoking.

Methods or Approach:

A 2 x 2 factorial design (use of gum and number of sessions) was employed. Patients, recruited from ordinary patients visiting physicians, were randomly assigned to the four groups. Thirteen physicians participated. Tobacco abstinence was the major dependent variable, with self-report validated with analysis of CO. After the study was completed, physicians and patients were interviewed about their experiences, e.g., patients were asked to rate their physicians' personality variables that might have been related to a successful smoking cessation experience.

Results to Date:

Long followup (3 months) showed a trend toward better results (<0.12) than short followup (2 weeks) and nicotine gum was significantly better than no gum in maintaining abstinence ($p<0.05$). Best outcomes were found in those receiving long followup and nicotine gum; 12-month abstinence was 27 percent. Other groups recorded (1) 22 percent abstinence for short followup and gum; (2) 15 percent for long followup and no gum; and (3) 3 percent for short followup and no gum.

Future Plans:

The effect of smoking cessation therapy delivered by nurses will be studied.

Project Dates:

January 1982–1983.

Financial Support:

Aktiebolaget Leo, Helsinborg, Sweden.

Reference:

Fagerstrom, K.-O. "Effects of Nicotine Chewing Gum and Follow-Up Appointments in Physician-Based Smoking Cessation." *Preventive Medicine* 13(5):517-527, September 1984.

0469. UNIVERSITY HOSPITAL, Department of Obstetrics and Gynecology, S-214 01 Malmo, Sweden.

Project Title:

Fetal Dynamics and Maternal Smoking.

Principal Investigators:

Gennser, G.; Sindberg-Eriksen, P.; Stale, H.

Objective:

To define the acute responses to maternal smoking (one cigarette after 12 hours abstinence) of the fetal cardiovascular, respiratory, and locomotor systems.

Methods or Approach:

Noninvasive studies of the fetus have utilized diagnostic ultrasound. Fetal heart rate has been measured with conventional cardiotachography; fetal breathing movements and gross movements have been measured with real-time scanning combined with time–distance recording. Cardiovascular function has been evaluated by quantification of the volume pulses in the large vessels of the fetus using a newly developed echo-tracking procedure that allows measurement of movements of echoes down to 15 µm with 1 KHz repetition frequency. Pulse waves, reflecting the instantaneous magnitude of the vessel diameter on two levels of the vessel, are analyzed by computer with respect to waveform and propagation velocity, yielding indirect information on cardiac stroke volume and peripheral resistance.

Results to Date:

After smoking, the mean heart beat intervals and short-term variability decreased transiently; the values of both were positively correlated with maternal circulating nicotine values before smoking. A significant increase in the rate of fetal breathing movements appeared together with a reduction in the short-term variability of breath-to-breath intervals. The number of episodes without fetal breathing or gross movements increased after smoking. In pulse waves in the fetal descending aorta, the apparent diastolic diameter and pulse amplitude increased, while the ascending part of the curve increased in slope and decreased in duration; the late decremental velocity was reduced. The propagation velocity of the pulse wave also increased transiently.

Future Plans:
Investigations have been performed on smoking women in uncomplicated pregnancy. The next phase of study will include investigation of women with intrauterine growth retardation and hypertension.

Project Dates:
January 1981–December 1986.

Financial Support:
Swedish Tobacco Company; University Hospital, Malmo, Sweden.

0470. UNIVERSITY HOSPITAL, Department of Occupational Medicine, S-581 85 Linkoping, Sweden.

Project Title:
Occupation, Smoking and Lung Cancer.

Principal Investigators:
Axelson, O.; Edling, C.; Dave, S.

Objective:
To identify and quantify the relative contribution of occupation and smoking in the causation of lung cancer.

Methods or Approach:
Selection of 62 cases and 198 matched controls was made from the hospital's lung and medical clinics. Information on occupation and smoking was obtained with other general information, and occupations were classified according to relationship with lung cancer. Rate ratio (RR), attributable cases (AC), and etiological fraction (EF) were calculated with 95 percent confidence interval (CI) by traditional statistical methods.

Results to Date:
There is a progressive increase of RR with increase in smoking, with the highest RR (5.16) in the heavy smoker category. RR was highest for mine workers and workers exposed to asbestos (RR, 3.3). EF for smoking and exposure to hazardous substances was 38 percent and 7.9 percent, respectively.

Future Plans:
The relationship of housing structure and smoking with lung cancer will be evaluated.

Project Dates:
December 1980–December 1984.

Financial Support:
WHO.

0471. UNIVERSITY OF GOTEBORG, OSTRA HOSPITAL, Department of Preventive Medicine, S-416 85 Gothenburg, Sweden.

Project Title:
The Project Preoperative Risk (PROPER)

Principal Investigators:
Svardsudd, K.; Wilhelmsen, L.; Ekstrom-Jodal, B., et al.

Objective:
To evaluate factors, in a defined population, that determine risk of complications during and after surgery.

Methods or Approach:
All patients undergoing elective surgery are evaluated at a preoperative outpatient clinic. A number of variables are recorded, including a detailed smoking history. About 6,000 patients will be followed during and after surgery by means of a special register organization in the operating room and postoperative ward.

Results to Date:
Data from a recently concluded pilot study (580 patients) show that smoking was one of several factors found that affect risk of postoperative complications. Final results are not yet available.

Project Dates:
March 1984–December 1987.

Financial Support:
University of Goteborg; Swedish Government.

0472. UNIVERSITY OF GOTEBORG, OSTRA HOSPITAL, Department of Preventive Medicine, S-416 85 Gothenburg, Sweden.

Project Title:
The Study of Men Born in 1913 and 1923.

Principal Investigators:
Svardsudd, K.; Larsson, B.; Welin, L., et al.

Objective:
To determine effects of smoking and other risk factors on incidence of cardiovascular and other diseases.

Methods or Approach:
The prospective population study of samples from the general population includes about 1,500 men who have been followed since 1963. Cohorts have been examined at 5-year intervals (the last time in 1980-1981) and information obtained on a large number of variables, including smoking habits and changes in smoking habits. Cause specific mortality, incidence of myocardial infarction and stroke, and cancer incidence are being followed and confirmed through official registers and death certificates.

Results to Date:
Data from earlier substudies have been published; most noted the importance of smoking in risk of acquiring cardiovascular disease, cancer (especially lung cancer), respiratory disease, and gastrointestinal disease. Results of a current investigation of the importance of smoking for development of pleural plaques among asbestos workers are not yet available. Factors associated with success in cessation of smoking in this population are also being identified.

Project Dates:
January 1963–continuing.

Financial Support:
University of Goteborg; MRC, Sweden.

0473. UNIVERSITY OF GOTEBORG, OSTRA HOSPITAL, Department of Medicine I, 416 85 Gothenburg, Sweden.

Project Title:
The Multifactor Primary Prevention Trial in Goteborg.

Principal Investigators:
Wilhelmsen, L.; Berglund, G.; Elmfeldt, D., et al.

Objective:
To determine whether multifactorial intervention against smoking, hypercholesterolemia, and hypertension will result in a decrease of coronary heart disease.

Methods or Approach:
The trial covered all male inhabitants in the city of Goteborg who were born between 1915 and 1922 and between 1924 and 1925 (47 to 55 years of age at entry to the study in 1970 to 1973). One-third were randomly allocated to an intervention

group; two-thirds acted as controls. The intervention group consisted of about 10,000 men and the control groups of about 10,000 men each (75 percent response rate). Groups were assumed to have had similar characteristics and risk factors were measured only in the intervention group at the start of the trial. Intervention comprised advice about diet (individually and in groups depending on level of serum cholesterol) and advice to stop smoking. Men with elevated blood pressure were treated with antihypertensive drugs. After 4 years, risk factor levels were checked in the intervention group and in an 11 percent random subsample of one control group. Levels were checked in the intervention group and 20 percent of one of the control groups after 10 years.

Results to Date:

Serum cholesterol, blood pressure, and smoking decreased among men in both the intervention and the control groups. Total serum cholesterol was 6.46 mmol/L at start and 6.04 mmol/L in the intervention group and 6.05 mmol/L in the control group after 10 years. Initially, 50.7 percent were smokers, but after 10 years, only 32.5 percent of the intervention group and 35.4 percent of controls were still smoking. After 10 years, 26 and 20 percent of the intervention and control groups, respectively, had been put on antihypertensive drug treatment, compared with 5.9 percent at the start of the trial. No significant effect on total or cardiovascular mortality or on incidence of myocardial infarction or stroke was found. A markedly higher mortality in the group of nonparticipants diluted results; total mortality was 22.3 percent among nonparticipants compared with 9.8 percent among participants. Some results of the trial, and data from other previous prospective studies in the same age groups in Goteborg, indicate a favorable trend with respect to coronary heart disease incidence and mortality during recent years.

Project Dates:

January 1970–1986.

Financial Support:

Swedish National Bank Tercentenary Fund.

0474. UNIVERSITY OF GOTEBORG, OSTRA HOSPITAL, Department of Medicine I, S-416 85 Gothenburg, Sweden.

Project Title:

Multivariate Analysis of Risk Factor for Myocardial Infarction, Stroke, Cancer, and Total Mortality Among Middle-Aged Men in Goteborg, Sweden.

Principal Investigators:

Wilhelmsen, L.; Berglund, G.; Elmfeldt, D., et al.

Objective:

To determine to what extent conventional risk factors, even if treated, are of importance for disease incidence in various populations.

Methods or Approach:

The intervention group of the Multifactor Primary Prevention Trial in Goteborg comprises a large population sample within a narrow age range (47 to 55 years of age). The cohort has been followed for coronary heart disease (CHD) and stroke incidence and cause specific mortality. Of special interest is the population attributable risk concept, especially when several risk factors are considered simultaneously. A total of 7,500 men were followed for a mean of 11.8 years.

Results to Date:

Data show that 575 men suffered a nonfatal or fatal CHD event, 134 had a nonfatal of fatal stroke, 214 died from cancer, and 195 died from other causes. Total mortality was 734 persons. CHD was found to be independently associated with elevated total serum cholesterol, tobacco smoking, elevated blood pressure, elevated relative body weight, low physical activity during leisure time, diabetes mellitus, alcoholic intemperance, and psychological stress. However, the last three factors accounted for less than 10 percent of CHD cases. Stroke events were significantly related to blood pressure, psychological stress, and smoking. Cancer mortality was significantly related only to tobacco smoking in multivariate analysis, and with alcohol intemperance in univariate analysis. Of all cancer cases, 24 percent were attributable to smoking. Other deaths were related to alcohol intemperance, smoking, low physical activity, and diabetes mellitus. Total mortality was significantly related to smoking, diabetes mellitus, alcoholic intemperance, elevated systolic blood pressure, elevated serum cholesterol, and low physical acitivity during leisure time.

Project Dates:

1970–1986.

Financial Support:

Swedish National Bank Tercentenary Fund.

0475. UNIVERSITY OF GOTHENBURG, Department of Environmental Hygiene, Box 33031, S-400 33 Gothenburg, Sweden.

Project Title:

Pulmonary Reactions After Exposure to Cigarette Smoke in Combination With Other Inhaled Agents.

Principal Investigators:

Rylander, R.; Sjostrand, M.

Objective:

To investigate cellular reactions in free lung cells in guinea pigs exposed to puffs of freshly generated cigarette smoke in subchronic inhalation experiments; study influence of simultaneous exposure to inhaled particulates, especially industrial dusts.

Methods or Approach:

Guinea pigs are exposed to one puff of freshly generated cigarette smoke in a dilution of 1:10 once every minute. Two cigarettes are given 5 days a week for several weeks. At the termination of exposure, pulmonary lavage is performed and differential count made of free lung cells. Histological sections of trachea are prepared and degree of irritation is determined by judging appearance of goblet cells. Lysosomal enzymes are measured in lung lavage fluid and in alveolar macrophages, cultured for 24 hours. lysosomal enzymes is measured after incubating these cells under in vitro conditions.

Results to Date:

In animals subacutely exposed to smoke only, a slight increase of lysosomal enzymes in cultured alveolar macrophages was detected. In animals where exposure to bacterial lipopolysaccharide (endotoxin, LPS) followed tobacco smoke exposure, the normal inflammatory response, in terms of invasion into the airways of neutrophils, was decreased and lysosomal enzymes in lung lavage compared with those exposed to LPS only. In animals exposed to asbestos (amosite) for 3 weeks, followed by 16 weeks of tobacco smoke exposure, an increase of macrophages, lymphocytes, and neutrophils was seen in the lungs and a slight increase of lysosomal enzymes in lung lavage fluid, as well as in cultured alveolar macrophages.

Future Plans:

The project will continue with combination exposures using other dusts; and other cell reactions, particularly the relationship between macrophages and neutrophils, will be investigated.

Project Dates:
1970–continuing.
Financial Support:
University of Gothenburg.

0476. UNIVERSITY OF LUND, SCHOOL OF DENTISTRY, Department of Oral Surgery, Specialisttandvarden, Regional Hospital, S-631 88 Eskilstuna, Sweden.

Project Title:
Epidemiologic Study of Excessive Oral Melanin Pigmentation With Special Reference to the Influence of Tobacco Habits.

Principal Investigators:
Axell, T.; Hedin, C.A.
Objective:
To study oral melanin pigmentation as to prevalence, distribution within the oral mucosa, and correlation to tobacco habits; to reject or confirm the earlier reported observation of tobacco smoking as the main cause of oral melanin pigmentation in Sweden (smokers' melanosis).
Methods or Approach:
In a clinical and histological examination undertaken in 20,333 inhabitants, oral mucosal lesions and oral melanin pigmentation were determined and statistical calculations were undertaken. Melanin pigmentation was correlated to mucosal region, sex, age, and tobacco consumption (duration, number of cigarettes, pipe smoking, snuff-dipping, cessation of smoking).
Results to Date:
Overall, 9.9 percent of subjects showed oral melanin pigmentation. Among tobacco smokers, 21.5 percent were pigmented compared with 3 percent of nonsmokers. Pigmentation was generally in the anterior gingiva of mandible and maxilla, but was also found in other regions. Significant differences were found in pigmented regions between cigarette smokers, pipe smokers, and snuff-dippers. The correlation between the number of cigarettes smoked and percent of pigmented individuals in the group was $r=0.98$. Female smokers were pigmented significantly more often than males in different cigarette consumption groups. Even one to three cigarettes increased pigmentation from 3 percent to 9.3 percent. Above 15 cigarettes/day, 30.5 percent of smokers were pigmented. Between 1 and 3 years after cessation of smoking, pigmentation disappeared. Pigmentation developed about 6 months after smoking initiation.
Future Plans:
Pigmentation in the 3 percent of nonsmokers will be investigated, including earlier tobacco smokers and southern Europeans in whom a genetically acquired oral melanin pigmentation is expected.
Financial Support:
Swedish Tobacco Company and County Council of Sodermanland.
Reference:
Hedin, C.A. "Smokers' Melanosis. Occurrence and Localization in the Attached Gingiva. *Archives of Dermatology* 133:1533-1538, 1977.

0477. UNIVERSITY OF STOCKHOLM, Department of Organic Chemistry, Arrhenius Laboratory, S-106 91 Stockholm, Sweden.

Project Title:
Studies of Nicotine Metabolites.

Principal Investigator:
Brandange, S.
Objective:
To gain information about the chemistry of nicotine and the reactions involved in its metabolism.
Methods or Approach:
Nicotine analogs or metabolites are being synthesized and then investigated by spectroscopic or enzymatic methods.
Results to Date:
A hydrodiperchlorate of nicotine $\Delta^{1'(5')}$-iminium ion has been synthesized. At pH 7.4, an aqueous solution of this salt contains the iminium ion and the corresponding carbinolamine in the approximate ratio 3:1. The second step in the metabolic conversion of nicotine to cotinine is an oxidation of this iminium ion mediated by aldehyde oxidase. Of several substrates for rabbit liver aldehyde oxidase, the nicotine iminium ion and a few other compounds show the lowest value of K_M.
Project Dates:
August 1974–continuing.
Financial Support:
Swedish Tobacco Company (8003; 8115).

SWITZERLAND

0478. ASSOCIATION DEPARTEMENTALE D'EDUCATION SANITAIRE ET SOCIALE DE L'ISERE, 23 Avenue Albert ler de Belgique, 38100 Grenoble, Switzerland.

Project Title:
Methodology of Health Education About Tobacco and Alcohol Addiction for Teenagers in Professional Training.

Principal Investigators:
Andre, E.; Delormas, P.; Scalliet, D., et al.
Objective:
To identify specific obstacles in teaching health education to an adolescent population that is being trained for manual and technical trades; suggest an educational program that takes such obstacles into account.
Methods or Approach:
The project will be carried out in three stages. (1) It will be within the field of epidemiological studies and in relation to the recent development of education through health in schools. (2) Behavior of pupils will be analyzed by bringing to light different problems linked to the school, community, and family environment. Difficulties and needs mentioned by educators will be identified, using a communication tool ("l'abaque de Regnier"), video-recorded and analyzed role-playing, and questions to establish consumption. (3) Methodology for intervention and experimentation will be developed.
Results to Date:
Resistance to health education is linked to a feeling of insecurity as to the future (mostly for boys), to a feeling of failure, and to pressure from schoolmates as a group. Educators want to develop talks and reflections on such matters instead of using traditional teaching. Based on findings, an educational program called TACALDO (tobacco-alcohol-adolescents) was developed that consists of (1) a training period for

teachers to make them familiar with techniques used by group leaders and to give them a better understanding of what adolescents go through in relation to attitudes toward alcohol and tobacco; (2) a period for arousing interest among students; (3) a period in which group leaders are in charge of students (an essential stage); (4) a learning period (answers to precise questions are required); and (5) a technique for smoking cessation, perfected for adolescents who request it. For each part of the program, education tools have been developed, including tests, self-questioning, and slide programs about tobacco and sports, sexuality, growth, lungs, and women.

Future Plans:
The TACALDO program will be set up on a regional scale (eight departments) and a technique will be perfected to help adolescents stop smoking.

Project Dates:
October 1984–December 1985.

Financial Support:
Secretariat d' Etat Charge de la Sante, Paris.

0479. BATTELLE, GENEVA RESEARCH CENTER, 7 route de Drize, CH-1227 Carouge, Geneva, Switzerland.

Project Title:
Respiratory Physiology.

Principal Investigators:
Coggins, C.R.E.; Musy, C.; Ventrone, R.

Objective:
To determine the effects of exposure to different tobacco smokes on the pulmonary physiology of rats.

Methods or Approach:
In vivo and in vitro tests of pulmonary physiology are made in animals during and at the end of exposures, using computer-controlled systems.

Results to Date:
Exposure to cigarette smoke reduces minute ventilation; other changes in pulmonary physiology are induced by subchronic exposures.

Project Dates:
1974–continuing.

References:
(1) Coggins, C.R.E. "Changes in the Respiratory Physiology of Rats Exposed to Different Phases of Cigarette Smoke." In: Sanders, C.L.; Cross, F.T.; Dagle, G.E.; Mahaffey, J.A. (Editors). *Pulmonary Toxicology of Respirable Particles.* 1980, pp. 420-430. (2) Coggins, C.R.E.; Musy, C.; Ventrone, R. "Changes in the Minute Ventilation of Rats Exposed to Different Concentrations of Cigarette Smoke." *Toxicology Letters* 11:181-185, 1982. (3) Ventrone, R.; Musy, C.; Coggins, C.R.E. "A Method for Producing Forced Expirograms in Laboratory Animals." *Laboratory Animals* 18:379-382, 1984.

0480. BATTELLE, GENEVA RESEARCH CENTER, 7 route de Drize, CH-1227 Carouge, Geneva, Switzerland.

Project Title:
Inhalation Toxicology.

Principal Investigators:
Coggins, C.R.E.; Fouillet, X.; White, R.

Objective:
To develop a smoke inhalation model which permits discrimination between different cigarettes on the basis of respiratory tract alterations.

Methods or Approach:
Animals are exposed to smoke in Battelle smoking machines. Respiratory tract alterations are examined using histopathology. Deposition patterns are verified using radiolabels and measurements of carboxyhemoglobin.

Results to Date:
Responses in the respiratory system are characterized by hyperplastic and metaplastic alterations, which permit distinguishing between different smoking products. The changes appear to be reversible.

Project Dates:
1974–continuing.

References:
(1) Baumgartner, H.; Coggins, C.R.E. "Description of a Continuous-Smoking Inhalation Machine for Exposing Small Animals to Tobacco Smoke." *Beitraege zur Tabakforschung International* 10(3):169-184, October 1980. (2) Coggins, C.R.E.; Fouillet, X.L.M.; Lam, R., et al. "Cigarette Smoke Induced Pathology of the Rat Respiratory Tract: A Comparison of the Effects of the Particulate and Vapour Phases." *Toxicology* 16:83-101, 1980. (3) Coggins, C.R.E.; Lam, R.; Morgan, K.T. "Chronic Inhalation Study in Rats, Using Cigarettes Containing Different Amounts of Cytrel Tobacco Supplement." *Toxicology* 22:287-296, 1982. (4) Musy, C.; Coggins, C.R.E. "A Program for Handling Data Obtained by 'Blind' Histopathological Evaluations." *International Journal of Biomedical Computing* 15:285-302, 1984. (5) Ringrose, A.; Crawlty, F.E.H.; Coggins, C.R.E. "An Automatic Device for the Addition of Precise Amounts of Radiolabel to Cigarettes." *Beitraege zur Tabakforschung International* 12:117-121, 1984.

0481. SWISS FEDERAL INSTITUTE OF TECHNOLOGY, INSTITUTE OF BEHAVIORAL SCIENCE, Department of Behavioral Biology, Turnerstrasse 1, ETH Zentrum, CH-8092 Zurich, Switzerland.

Project Title:
Situational Influences on Cigarette Puffing and Inhalation.

Principal Investigators:
Nil, R.; Battig, K.

Objective:
To investigate patterns of cigarette puffing and inhalation and alveolar carbon monoxide (CO) boost under different stressful conditions.

Methods or Approach:
The experiment is performed according to a repeated measure design, involving four different 60-minute laboratory test sessions with each subject. The four conditions are nonstressful video film (control condition), fixed interval reinforcement schedule (button pressing for money), selective attention task, and noise stress. Dependent variables include patterns of puffing and inhalation, alveolar CO uptake, and smoking-induced pulse rate reactivity.

Results to Date:
Project is in a preliminary phase.

Project Dates:
June 1984–March 1985.

Financial Support:
Swiss Association of Cigarette Manufacturers.

0482. SWISS FEDERAL INSTITUTE OF TECHNOLOGY, INSTITUTE OF BEHAVIORAL SCIENCE, Department of Behavioral Biology, Turnerstrasse 1 ETH-Zentrum, CH-8092 Zurich, Switzerland.

Project Title:
Visual Evoked Potentials in Rapid Information Processing.

Principal Investigators:
Michel, C.; Nil, R.; Battig, K.
Objective:
To investigate evoked EEG potentials during a visual rapid information processing test in groups of regular smokers under smoking and nonsmoking conditions.
Methods or Approach:
Two 30-min runs of rapid information processing will be utilized in a 2 x 2 crossover research design. Groups will be smoking deprived or undeprived before the experiment and allowed to smoke or not between runs. The task consists of responding to triads of either even or odd successive digits presented on a screen. Speed of digit presentation will automatically be adapted to actual performance level. Digit presentation onset will serve as the trigger signal for measurement of visual evoked potential.
Results to Date:
Project is in a preliminary phase.
Project Dates:
May 1984–March 1986.
Financial Support:
Swiss Association of Cigarette Manufacturers.

0483. SWISS FEDERAL INSTITUTE OF TECHNOLOGY, INSTITUTE FOR BEHAVIORAL SCIENCES, Department of Behavioral Biology, Turnerstrasse 1, CH-8092 Zurich, Switzerland.

Project Title:
Effects of Smoking on Vegetative Reactivity to Noise in Light Versus Deep Inhalers.

Principal Investigators:
Woodson, P.P.; Buzzi, R.; Nil, R., et al.
Objective:
To clarify the role played by nicotine in stress reduction in different types of smokers (light vs. deep inhalers).
Methods or Approach:
Two groups of smokers were selected: 12 light inhalers who showed average pre/postsmoking carbon monoxide (CO) boost in respiratory tidal air of ≤ 1.0 ppm, and 12 deep inhalers who typically exhibited CO boosts of ≥ 3.0 ppm. Groups were compared in an experiment involving psychophysiological stress reactivity to intermittent environmental noise bursts (95 dBA peak intensity) before and after smoking, following 15 hours of deprivation. Degree of subjective stress was reported after each noise burst in deviations from that experienced during the first burst. Electrocardiogram, photoplethysmogram, pulse transit time, electromyogram, respiration, and skin conductance were recorded continuously.
Results to Date:
Light inhalers apparently derive a greater stress-dampening effect from less nicotine than deep inhalers derive from more, which would indicate that light inhalers use nicotine more efficiently than deep inhalers for protection against stress.
Project Dates:
June 1983–December 1984.
Financial Support:
Forschungsgesellschaft Rauchen und Gesundheit, West Germany.

0484. SWISS FEDERAL INSTITUTE OF TECHNOLOGY, INSTITUTE OF BEHAVIORAL SCIENCE, Department of Behavioral Biology, Turnerstrasse 1, ETH-Zentrum, CH-8092 Zurich, Switzerland.

Project Title:
Smoking, Selective Attention and Auditory Evoked EEG-Potentials.

Principal Investigators:
Battig, K.; Michel, C.; Nil, R.
Objective:
To investigate interactive effects of smoking and attention in an auditory selective attention task.
Methods or Approach:
A two-by-two crossover design will be used, with deprivation and nondeprivation and smoking and nonsmoking conditions. Pure tones will be delivered (in rapid irregular sequences) and randomly distributed to both ears. The selective attention task will be to concentrate on one ear only and to count irregularly interspersed target tones.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–March 1986.
Financial Support:
Swiss Association of Cigarette Manufacturers.

0485. SWISS FEDERAL INSTITUTE OF TECHNOLOGY, INSTITUTE OF BEHAVIORAL SCIENCE, Department of Behavioral Biology, Turnerstrasse 1, ETH Zentrum, CH-8092 Zurich, Switzerland.

Project Title:
Characterisation of Regularly Inhaling and Noninhaling Smokers.

Principal Investigators:
Battig, K.; Nil, R.; Woodson, P.P.
Objective:
To select regularly inhaling and noninhaling smokers by means of alveolar carbon monoxide (CO) absorption when smoking habitual cigarettes; compare them for puffing and inhalatory patterns and for questionnaire ratings including personality scores, aspects of coronary prone behavior pattern (Type A), lifestyle, and consumatory habits.
Methods or Approach:
Out of a sample of 171 regular smokers, 19 inhalers and 20 noninhalers were selected as smokers with smoking-induced tidal air CO boost of < 1 ppm or of > 3 ppm in each of three independent test sessions. Puffing patterns were quantitatively recorded by a pressure and flow device and inhalatory patterns by concomitant spirometrically calibrated respiratory trace.
Results to Date:
Inhalers differed from noninhalers by daily cigarette consumption and latencies to the first cigarette of a day, but not for machine standard smoke yields of cigarettes. Among the consumatory indexes, differences were found for alcohol consumption, consumption of pills and tablets, and coffee consumption. No differences were found for classical personality dimensions (Eysenck) or for coronary-prone behavior.
Future Plans:
The two groups of smokers will be further compared for puffing behavior and smoking-induced pulse reaction after different deprivation periods.
Project Dates:
June 1982–December 1984.

0486. SWISS FEDERAL INSTITUTE OF TECHNOLOGY, INSTITUTE OF BEHAVIORAL SCIENCE, Department of Behavioral Biology, Turnerstrasse 1, ETH-Zentrum, CH-8092 Zurich, Switzerland.

Project Title:
Effects of Nicotinic and Non-Nicotinic Activation on the Vegetative Reactivity to Noise.

Principal Investigators:
Battig, K.; Nil, R.
Objective:
To determine whether patterns of noise reactivity seen during smoking also occur in nonnicotinic cardiovascular activation situations (physical activity and mental loads).
Methods or Approach:
The experiment, performed according to a repeated measure design, will include the following four test sessions: smoking a personal brand cigarette, performing a mild physical activity, performing a letter cancellation test, and performing the Stroop conflict learning test. Within a test session, three preactivity noise bursts of 36 sec each every 3 minutes (baseline) will be followed by five subsequent noise bursts after treatment (smoking, physical, or mental stress).
Results to Date:
Project is in a preliminary phase.
Project Dates:
May 1985–March 1986.
Financial Support:
Swiss Association of Cigarette Manufacturers.

0487. SWISS FEDERAL INSTITUTE OF TECHNOLOGY, INSTITUTE OF BEHAVIORAL SCIENCE, Department of Behavioral Biology, Turnerstrasse 1, ETH Zentrum, CH-8092 Zurich, Switzerland.

Project Title:
Effect of Smoking Deprivation on Regularly Inhaling and Noninhaling Smokers.

Principal Investigators:
Battig, K.; Woodson, P.P.; Nil, R.
Objective:
To investigate patterns of puffing and inhalation, tidal air carbon monoxide (CO) boosts, and smoking-induced pulse acceleration in two preselected groups of inhaling and noninhaling smokers who depend differentially on the pharmacological properties of nicotine.
Methods or Approach:
The study included three different test sessions according to an experimental design, which allowed pairwise comparisons of smoking behavior under control and deprivation conditions (1 hour, 2 hours, and 13 hours). Subjects smoked habitual cigarettes, and puffing patterns were recorded with a pressure and flow device and inhalation patterns by the concomitant spirometrically calibrated registration of respiratory trace. Pulse rate was continuously monitored, and mixed expiratory tidal air was analyzed for CO concentration before and after smoking.
Results to Date:
Group differences were as expected for tidal CO boost under all conditions. A differential picture for the two groups was obtained in reaction to the different deprivation conditions for presmoking pulse rate, smoking-induced pulse reaction, and tidal CO boost.
Future Plans:
The two groups of smokers will be further compared for rapid information processing and effects of smoking on vegetative reactivity to noise.
Project Dates:
June 1982–December 1984.

0488. SWISS INSTITUTE FOR EXPERIMENTAL CANCER RESEARCH, Ch. des Boveresses, 1066 Epalinges, Switzerland.

Project Title:
Chromosomal Damage by Components of Tobacco Smoke.

Principal Investigator:
Cerutti, P.A.
Objective:
To elucidate the mechanisms of action of carcinogenic components in tobacco smoke, concentrating on the promotion phase of tobacco-induced carcinogenesis where the intermediate formation of active oxygen appears to play an important role.
Methods or Approach:
The program is divided into three subprojects: (1) development of a test system for detection of chromosomal damaging agents in cigarette smoke that operate by indirect action, including formation of DNA strand breakage; (2) tumor promotion-related modulation of gene expression, as exemplified by induction of poly ADP-ribosylation of chromosomal proteins in response to tumor promoters; and (3) membrane-active components in cigarette tar, particularly the effect of benzo (*a*)pyrene on arachidonic acid metabolism in human monocytes.
Results to Date:
Appropriate technologies have been developed for all subprojects. Data obtained for project 2 indicate that phorbol-ester promoter TPA induces poly ADP-ribosylation in fibroblast cultures via intermediate formation of active oxygen.
Project Dates:
January 1984–December 1986.
Financial Support:
Swiss Association of Cigarette Manufacturers.

0489. UNIVERSITY HOSPITAL, Department of Internal Medicine, Medical Policlinic, Raemistrasse 100, 8091 Zurich, Switzerland.

Project Title:
Smoking Patterns of Smokers With and Without Tobacco-Smoke Related Lung Diseases.

Principal Investigator:
Medici, T.C.
Objective:
To determine whether the pattern of smoke inhalation (the way smoke is inhaled) differs among smokers with tobacco-related lung diseases.
Methods or Approach:
On the basis of clinical and radiological findings and pulmonary function tests, 91 smokers were classified as smokers without lung diseases, or with small airway disease, simple chronic bronchitis, obstructive chronic bronchitis, pulmonary emphysema, or lung cancer. Smoking and breathing patterns were recorded, using a smoke flow machine and strain gauge belt while subjects smoked a cigarette. Blood levels of carboxyhemoglobin were determined before and after smoking.
Results to Date:
Puff inhalation time, puff peak pressure, and the venous difference in COHb level before and after smoking varied significantly among groups. Puff inhalation time (duration of smoke retention in the mouth) was only 0.08 seconds in

smokers with pulmonary emphysema, significantly different from the time in other groups. This puffing characteristic may be the consequence or the cause of emphysema. If the latter is true, smokers with emphysema may lack the acute airway response to smoke inhalation that normally protects most smokers from immediately inhaling smoke.

Future Plans:
Further studies will be conducted on more subjects to confirm preliminary findings and young smokers with short puff inhalation times will be prospectively monitored to determine whether they develop emphysema.

Project Dates:
October 1980–1986.

Financial Support:
University Hospital, Zurich; Swiss Association of Cigarette Manufacturers.

Reference:
Medici, T.C.; Unger, S.; Ruegger, M. "Smoking Pattern of Smokers With and Without Tobacco-Smoke Related Lung Diseases." *American Review of Respiratory Disease* (In press).

0490. UNIVERSITY INSTITUTE OF SOCIAL AND PREVENTIVE MEDICINE, Gloriastrasse 30, CH-8006 Zurich, Switzerland.

Project Title:
Follow-Up Study on Smoking Habits After Pregnancy.

Principal Investigators:
Lang, F.; Steffen, R.; Schar, M.

Objective:
To assess the proportion of women who start smoking after pregnancy; evaluate possible reasons for starting to smoke.

Methods or Approach:
A questionnaire survey will be conducted to determine smoking habits of women after pregnancy.

Results to Date:
Project is in a preliminary phase.

Project Dates:
March 1984–December 1985.

Financial Support:
University Institute of Social and Preventive Medicine, Switzerland.

0491. UNIVERSITY INSTITUTE OF SOCIAL AND PREVENTIVE MEDICINE, Gloriastrasse 30, CH-8996 Zurich, Switzerland.

Project Title:
Critical Assessment of Various Methods Used to Stop Smoking.

Principal Investigator:
Steffen, R.

Objective:
To analyze the various methods used to stop smoking that are available in Switzerland.

Methods or Approach:
A literature review was used to assess the various methods available.

Results to Date:
Documentation on the various methods is incomplete and therefore not entirely reliable. However, while none of the methods guarantees success, practicing physicians should not surrender. If each physician persists in attempting to convince smokers to quit, 80,000 persons a year could become nonsmokers in Switzerland.

Project Dates:
May 1983–January 1984.

Financial Support:
University Institute of Social and Preventive Medicine, Switzerland.

0492. UNIVERSITY OF BERN, Department of Social and Preventive Medicine, Finkenhubelweg 11, CH-3012 Bern, Switzerland.

Project Title:
Epidemiological Analysis of Hospital Diagnosis Data.

Principal Investigators:
Abelin, T.; Ehrengruber, H.

Objective:
To (1) analyze hospital diagnosis data; (2) extrapolate to the country as a whole and to socio-culturally different regions; (3) compute cancer incidence for all major sites; and (4) analyze correlations with personal and regional characteristics.

Methods or Approach:
For most cancer sites, patients are admitted to a hospital at some point of the disease process. Analysis of country-wide hospital diagnosis statistics thus allows for insights into time trends of cancer incidence by regions and socio-demographic characteristics. Emphasis will be on cancer sites known to be associated with tobacco and/or alcohol consumption. Data will be drawn from the VESKA-hospital diagnosis statistics system, which has been in existence since 1969, and today includes 309 hospital departments with approximately 300,000 yearly admissions.

Results to Date:
Methods of record linkage and of extrapolation have been developed. Data analysis is in progress.

Project Dates:
1984–1986.

Financial Support:
Swiss National Science Foundation; Swiss Hospital Association (VESKA).

0493. UNIVERSITY OF BERN, Department of Social and Preventive Medicine, Finkenhubelweg 11, CH-3012 Bern, Switzerland.

Project Title:
Evaluation of a Self-Instructional Manual for Smoking Cessation in Switzerland.

Principal Investigator:
Abelin, T.

Objective:
To conduct a retrospective evaluation of acceptance and effectiveness of a self-instructional manual for smoking cessation in different parts of the population.

Methods or Approach:
In 1982, a German language version of the American Lung Association's instructional manuals "Freedom From Smoking in 20 Days" and "A Lifetime of Freedom From Smoking" were introduced in Switzerland. Distribution was by mail order and through bookstores. A postal questionnaire will be sent to all mail-order recipients of the manual, asking for information about smoking habits and how the manual was used. Detailed interviews with a subsample of respondents and telephone inquiries with nonrespondents are planned.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Results will be used to choose appropriate target populations for further editions of this or similar manuals.
Project Dates:
November 1984–July 1986.
Financial Support:
University of Bern; Swiss Association Against Tuberculosis and Lung Diseases.

0494. UNIVERSITY OF ZURICH, PSYCHIATRIC CLINIC, Research Directorate, Box 68, CH-8029 Zurich, Switzerland.

Project Title:
Epidemiology and Etiology of Illicit Drugs, Alcohol and Tobacco Consumption: A Longitudinal Study.

Principal Investigators:
Sieber, M.F.; Angst, J.
Objective:
To (1) describe patterns of tobacco consumption in males at age 31 and changes in consumption over a 12-year period; (2) compare cigarette smokers with increased consumption with those with constant or decreased consumption in regard to demographic background, personality, and social attitudes; and (3) predict level of consumption at age 31 with information collected 12 years earlier.
Methods or Approach:
In the longitudinal study, 1,577 males were questioned in 1971 (at age 19) and in 1983 (at age 31). The followup sample consists of 55 percent of the original representative sample collected 12 years earlier. Bivariate analysis, multiple regression analysis, and path analysis will be used to analyze data.
Results to Date:
Point prevalence of smoking decreased slightly, from 48.1 percent at age 19 to 46.7 percent at age 31. Pipe smoking increased from 13.5 percent to 21.3 percent and cigar smoking from 2.5 percent to 20.4 percent at followup. Average number of cigarettes smoked/day increased from 14.1 to 16.8; however, total tobacco consumption remained almost stable at 16.5 g tobacco/day for smokers and 9.3 g tobacco/day for the whole sample (1982).
Future Plans:
Data analysis will continue, for prediction of later cigarette consumption and identification of risk factors for cigarette consumption.
Project Dates:
1981–December 1985.
Financial Support:
University of Zurich; Swiss National Foundation for Scientific Research (3.887.0.81).

0495. UNIVERSITY OF ZURICH, INSTITUTE OF PATHOLOGY, Cancer Registry of the Canton of Zurich, Schmelzbergstrasse 12, CH-8091 Zurich, Switzerland.

Project Title:
Epidemiology of Lung Cancer in Switzerland.

Principal Investigator:
Schuler, G.
Objective:
To assess the impact and causes of the frequency of lung cancer in Switzerland.
Methods or Approach:
Methods include (1) statistical analysis of lung cancer trends and geographical distribution of mortality data; (2) analysis of mortality statistics by occupation; (3) analysis of a case–control study on lung cancer; (4) comparison of data with international literature; and (5) analysis of files of workers who died from silicosis.
Results to Date:
An overview on the epidemiology of lung cancer, with special reference to Switzerland has been published. Data from analysis of causes of death among silicotics was presented at the conference on silica and cancer in Chapel Hill, North Carolina, in April 1984. Excess risks of lung cancer found in miners and foundry workers could not be fully explained by the high prevalence of smoking among these occupations. Data from the case–control study of lung cancer are being analyzed. Frequency of lung cancer in Switzerland is being analyzed by regions, cohorts, and occupations. The increase in male lung cancer rates is not restricted to men over the age of 55, but a decline in younger age classes has not yet been clearly seen. Female lung cancer rates are increasing. The overall male/female ratio of lung cancer deaths is 6:2, but in those aged 35 to 44, the ratio is now at 2:0.
Project Dates:
1980–1986.
Financial Support:
University of Zurich.

0496. WORLD HEALTH ORGANIZATION, WHO SMOKING AND HEALTH PROGRAMME, WHO, 1211 Geneva 27, Switzerland. ADDICTION RESEARCH FOUNDATION, 33 Russell Street, Toronto, Ontario M5S 2S1, Canada.

Project Title:
Tar and Nicotine Analyses of Cigarettes From Developing Countries.

Principal Investigators:
Frecker, R.; Masironi, R.
Objective:
To assist developing countries in assessing level of tar and nicotine in cigarettes being marketed; provide guidance in carrying out analyses and in establishing national or regional analytical laboratories.
Methods or Approach:
Representative samples of best-selling brands, both locally produced and imported, have been collected according to a standardized protocol. Packets are airmailed to the central analytical laboratory at the Addiction Research Institute in Toronto for analysis.
Results to Date:
Partial results are described in a WHO report. It is expected that all results will be available in 1985 and that conclusions will be made.
Future Plans:
Emphasis will be on encouraging developing countries in setting up national or regional laboratories for cigarette analysis.
Project Dates:
1983–1985.
Financial Support:
Swedish International Development Agency.

TAHITI

0497. INSTITUT TERRITORIAL DE RECHERCHES MEDICALES LOUIS MALARDE, B.P. 30, Papeete, Tahiti. INSERM UNIT 179, 44 Chemin de Ronde, 78110 Le Vesinet, France.

Project Title:
Normal Standards of Some Parameters of Lung Function by Measure of Maximal Expiratory Flow-Volume Curve: Variability and Effects of Age, Sex, Height, and Race Among Schoolteenagers in French Polynesia.

Principal Investigators:
Chansin, R.; Neukirch, F.; Perdrizet, S., et al.

Objective:
To determine normal standards of lung function for the three races of French Polynesia: Polynesian (Maohi), Caucasian (French), and Chinese; develop better understanding of respiratory symptoms or diseases and smoking habits among youths aged from 10 to 20 years.

Methods or Approach:
The epidemiological survey is being conducted in schools in the urban areas of Tahiti. Self-administered questionnaires from 8,000 adolescents will provide information, with special reference to respiratory symptoms and diseases, smoking habits, and racial origins. A sample of 3,000 normal students (including smokers) will be selected to perform forced expiratory maneuvers. Spirometry, maximal expiratory flow-volume curves, and peak expiratory flow will be recorded for statistical analysis. Data obtained will be used for early detection of airflow obstruction. Questionnaire information will be compared with results of a 1979 survey of students aged 14 to 20 years.

Results to Date:
Project is in a preliminary phase.

Future Plans:
A similar survey of adults is planned.

Project Dates:
March 1984–December 1986.

Financial Support:
Institut Territorial de Recherches Medicales Louis Malarde, Tahiti; INSERM.

THAILAND

0498. MAHIDOL UNIVERSITY, FACULTY OF DENTISTRY, Department of Oral Pathology, Yothee Street, Phyathai, Bangkok 10400, Thailand.

Project Title:
Ultrastructural and Histological Alterations Produced by the Extracts of Betel Nut and Cured Tobacco on the Mucosa of Hamster Cheek Pouch.

Principal Investigators:
Weerapradist, W.; Tanpairoj, S.

Objective:
To study the histological and ultrastructural alterations of the mucosa of hamster cheek pouch produced by extracts of betel nut and cured tobacco; examine quantitative change in dark cells of the mucosa.

Methods or Approach:
Seventy-two male Syrian golden hamsters were divided into four equal groups and painted on the left cheek pouch three times/week by the following agents: (1) dimethyl sulfoxide, (2) extracts of betel nut, (3) extracts of tobacco, and (4) extracts of betel nut and tobacco (1:1). Animals in each group were were sacrificed at weeks 5, 10, 15, 20, 25, and 30, and the left cheek pouches were removed for examination.

Results to Date:
Results are not yet available.

Project Dates:
October 1983–October 1984.

Financial Support:
Mahidol University, Thailand.

TURKEY

0499. ANKARA NUCLEAR RESEARCH AND TRAINING CENTER, Besevler, Ankara, Turkey. MIDDLE EAST TECHNICAL UNIVERSITY, Department of Chemical Engineering, Ankara, Turkey.

Project Title:
Trace Elements in Turkish Tobacco Determined by Instrumental Neutron Activation Analysis.

Principal Investigators:
Gulovali, M.G.; Gunduz, G.

Objective:
To determine concentration of 20 trace elements in nine different brands of Turkish cigarette tobacco, in a brand of pipe tobacco, and in tobacco ash.

Methods or Approach:
Cigarette wrappers were removed and combined tobacco of each brand was mixed. Tobaccos were dried and samples pressed into pellets. Three brands were ashed at 900° C (without wrapping papers). NBS standard coal was used as a multielement comparison standard. Pelletized tobacco, standard samples, and ash samples were stacked in polyethylene tubes. Tubes were heat sealed, irradiated for 4 hours, and activities measured. Cooling and counting times were arranged according to nuclear properties of radioisotopes.

Results to Date:
Concentrations of potassium and bromine in pipe tobacco are one-half those found in cigarette tobaccos. Values for hafnium, chromium, zinc, sodium, and iron are almost twice those of cigarette tobaccos. Factors responsible are genetic variations,

differences in soil type, leaf stalk position, and saucing material added to pipe tobacco (which may contain up to 30 percent of materials such as licorice, sweetening agents, sugars, and other flavorants). Neutron activation analysis of cigarette tobaccos shows that almost all elements are present in about the same amounts. Comparisons with American and Iranian tobaccos show that arsenic concentrations are higher in American cigarettes and undetectable in Iranian brands. A large proportion of trace elements in cigarette tobacco is left in the ash, with only a small fraction transferred to smoke.

Reference:

Gulovali, M.C.; Gunduz, G. "Trace Elements in Turkish Tobacco Determined by Instrumental Neutron Activation Analysis." *Journal of Radioanalytical Chemistry* 78(1):189-198, 1983.

0500. UNIVERSITY OF ANKARA, DEPARTMENT OF PHARMACOLOGY, Sihhiye, Ankara, Turkey.

Project Title:

Inhibition by Nicotine of the Production of Prostacyclin in Kidney, Lung, and Coronary Vascular Bed.

Principal Investigators:

Turker, R.K.; Zengil, H.; Ercan, Z.S., et al.

Objective:

To (1) investigate the relationship between cigarette smoke and prostacyclin level in the increased incidence of cardiovascular diseases in smokers; (2) study effect of nicotine on cardiovascular homeostasis; and (3) determine relationship between decreased production of prostacyclin and increased synthesis of thromboxane A_2.

Methods or Approach:

One of the major active substances in tobacco is nicotine, which has been shown to be inhibited by prostacyclin synthetase in the vascular wall, thereby facilitating the production of atheromatous plaques in the arterial wall. Experiments were performed on isolated perfused organs from different species. The activity of prostacyclin and thromboxane A_2 was measured by bioassay. Radioimmunoassays were recently started on hospitalized patients. Blood samples were taken from the coronary sinus and left coronary artery; platelet functions were also determined, measuring aggregation by different stimuli (ADP, collagen, thrombin, arachidonic acid, epinephrine).

Results to Date:

In patients with ischemic heart disease, a very low level of prostacyclin was found in coronary blood samples. In contrast, thromboxane A_2 level was extremely high. In chronic smokers, the ratio of prostacyclin/thromboxane A_2 was lower than in nonsmokers. The ratio gradually increased following low doses of aspirin (110 mg/day), dipyridamol (75 mg/day), and propranolol.

Project Dates:

November 1980–November 1985.

Financial Support:

Turkish Scientific and Technical Research Council (TAG-480).

References:

(1) Turker, R.K. "Evidence for a Prostacyclin-Mediated Chronotropic Effect of Angiotensin II in the Isolated Cat Right Atria." *European Journal of Pharmacology* 83(3/4):271-275, September 24, 1982. (2) Turker, R.K.; Ercan, Z.S.; Ersoy, A., et al. "Inhibition by Nicotine of the Vasodilator Effect of Bradykinin: Evidence for a Prostacyclin-Dependent Mechanism." *Archives Internationales de Pharmacodynamie et de Therapie* 257(1):94-103, May 1982. (3) Ercan, Z.S.; Zengil, H.; Akar, F., et al. "Possible Prostacyclin-Mediated Vascular Effect of Angiotensin II in the Isolated Perfused Rat Lung." *Prostaglandins Leukotrienes and Medicine* 12(1):77-83, September 1983.

UNION OF SOVIET SOCIALIST REPUBLICS

0501. ALL-UNION CARDIOLOGICAL RESEARCH CENTER, Petroverigsky Pereulok 10, Moscow 101837, Union of Soviet Socialist Republics.

Project Title:

Psychological Characteristics of Heavy Smokers.

Principal Investigators:

Nemtzov, A.A.; Rojanetz, R.V.

Objective:

To investigate the microenvironment of heavy smokers; evaluate degree of disadaptation of heavy smokers to different spheres of the microsocial environment.

Methods or Approach:

In the primary investigation stage, a color test and incomplete sentence test are used. In the in-depth investigation, a complex psychosocial questionnaire, 16 PF (Cattell), clinical diagnosis of self-esteem, standard semantic differential of Feldes, and questionnaire test of motivation are employed. It is hypothesized that the psychological disadaptation of heavy smokers, which is anticipated, is a neurotic or subneurotic disorder, accentuated by personal characteristics.

Results to Date:

Project is in a preliminary phase.

Future Plans:

Data will be used in developing a psychotherapeutic program for prevention/intervention.

Project Dates:

May 1984–September 1986.

Financial Support:

All Union Cardiological Research Center, USSR.

0502. INSTITUTE OF PREVENTIVE CARDIOLOGY, Laboratory of Juvenile Hypertension, 10 Petroverigsky Lane, Moscow 101837, Union of Soviet Socialist Republics.

Project Title:

Epidemiological and Preventive Studies of Atherosclerosis and Coronary Heart Disease Precursors in Children and Adolescents.

Principal Investigators:

Alexandrov, A.A.: Prokhorov, A.V.

Objective:

To evaluate efficacy of preventive measures directed at reducing smoking prevalence in schoolchildren.

Methods or Approach:

A total of 2,300 schoolchildren in fifth grade (both sexes), residing in two Moscow communities, were screened in

October-November 1983. The following tests were applied: smoking questionnaire, blood pressure and pulse rate measurement, and anthropometry parameters. One community was the intervention group; the other served as a reference (control) community. At the same time, 542 students in grades 5 to 10 in one intervention school were examined in a similar manner, and a matching contingent was screened in a control area school, where spirometry was also conducted. Preventive actions were at three levels; pupils, parents, and teaching staff. A final examination will be conducted after the second year of intervention.

Results to Date:

Results are not yet available.

Future Plans:

A comparative study of serum thiocyanate levels and carbon monoxide in expired air will be conducted to validate questionnaire data on cigarette smoking by schoolchildren. Plans include introduction of recently developed prevention measures (such as use of peer leaders) to assess efficacy.

Project Dates:

October 1983–1986.

Financial Support:

Institute of Preventive Cardiology, Laboratory of Juvenile Hypertension, Union of Soviet Socialist Republics.

0503. INSTITUTE OF PREVENTIVE CARDIOLOGY, Laboratory of Juvenile Hypertension, 10 Petroverigsky Lane, Moscow 101837, Union of Soviet Socialist Republics.

Project Title:

Smoking Control Among Higher Students (Actions for Early CVD Prevention).

Principal Investigators:

Shamarin, V.M.; Timofeeva, S.G.

Objective:

To evaluate efficacy of prevention measures directed at reducing smoking prevalence in students in higher institutions.

Methods or Approach:

An examination will be conducted of first year students from two institutions of higher education in Moscow (3,500 students, both sexes). Tests will include smoking questionnaire, blood pressure measurement, anthropometry parameters, serum thiocyanate determination, and measurement of carbon monoxide in expired air. Subjects will be reexamined annually and biannually. An intervention is planned that will be carried out in various groups by various approaches in one institution with 2,500 students. The other institution (1,000 students) will be the control group.

Results to Date:

Results are not yet available.

Future Plans:

Plans include examination of respiratory function in smokers and nonsmokers to reveal early smoking-induced changes and to assess any association of smoking with other risk factors for coronary heart disease in the study population.

Project Dates:

December 1984–1987.

Financial Support:

Institute of Preventive Cardiology, Union of Soviet Socialist Republics.

UNITED KINGDOM

England.

0504. INSTITUTE OF PSYCHIATRY, Addiction Research Unit, 101 Denmark Hill, London SE5 8AF, England.

Project Title:

Social Psychological Investigations of Smoking and Other Health-Related Behaviours.

Principal Investigators:

Sutton, S.R.; Hallett, R.

Objective:

To (1) assess experimentally effects of videotapes about smoking and other health topics on attitudes, beliefs, intentions, and behavior; (2) investigate how effects on intentions and behavior are mediated (i.e., to understand processes of attitude change and decisionmaking); and (3) develop and evaluate minimum smoking intervention programs at workplaces.

Methods or Approach:

In field experiments, groups of employees are randomly assigned to watch one of a number of videotapes. Attitudes, beliefs, and intentions are measured by questionnaires, and self-reports of behavior are obtained in the short-term (3 to 4 months) and long-term (1 year), with validation by expired air carbon monoxide. Usefulness of two competing models of persuasion are compared; one based on amount of fear aroused by the videotape, the other on cognitive factors that might enter into the smoker's decision. In some instances, nicotine chewing gum is used as an adjunct to the videotapes.

Results to Date:

Preliminary results for the six studies that have been completed indicate that the videotapes used were not differentially effective in changing smoking behavior. However, regardless of which tape was seen, participants did better than nonparticipants.

Project Dates:

February 1980–September 1988.

Financial Support:

MRC, United Kingdom.

Reference:

Sutton, S.R.; Hallett, R. "Smoking Intervention at Places of Work Using Motivational Videotapes." In: Proceedings of the Fifth World Conference on Smoking and Health, Winnipeg, Canada, July 1983 (In press).

0505. ACTION OF SMOKING AND HEALTH, UNITED KINGDOM, Tower House, 7/11 Mortimer Street, London W1N, England.

Project Title:
The Role of Cigarette Advertising and Low Tar Cigarettes in the Initiation of Smoking in Children, and in Promoting Sex Differences in Smoking Trends.

Principal Investigator:
Jacobson, B.
Objective:
To investigate sex differences in adolescents' knowledge, perceptions, and smoking behavior in relation to low-tar cigarettes and advertising; examine sex differences in self-image and prevailing attitudes of smokers and nonsmokers, and correlate results with brand choice and perception.
Methods or Approach:
Research (by an opinion research company) will be qualitative and quantitative, involving pre- and post-discussion questionnaires to provide accurate background information on smoking behavior. Subjects will be 80 adolescents aged 15 to 16, recruited by a qualified interviewer. Participants will be divided into discussion minigroups according to demographic characteristics, with equal numbers of smokers and nonsmokers. The qualitative phase will be based on taped interviews covering awareness of brands and tar ratings, and images attributed to the brands, and influence of others (e.g., parents and siblings) in brand choice. The quantitative phase will include a questionnaire on current smoking behavior, preferred brand, and parental and friends' smoking behavior.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–April 1985.
Financial Support:
Cancer Research Campaign, United Kingdom.

0506. ADDENBROOKE'S HOSPITAL, Department of Respiratory Physiology, Chest Clinic, Hills Road, Cambridge, England.

Project Title:
The Deposition of Constituents of Cigarette Smoke in the Lungs.

Principal Investigators:
Woolman, P.; Cracknell, N.G.; Harmes, K., et al.
Objective:
To determine the site in the lung of deposition of various constituents of tobacco smoke.
Methods or Approach:
Proposed methods include radioactive labeling of smoke constituents and use of aerosol generators to determine site of deposition in the lung.
Results to Date:
Project is in a preliminary phase.
Future Plans:
A wide range of constituents will be studied and a model of lung deposition will be constructed.
Project Dates:
January 1985–January 1987.
Financial Support:
British American Tobacco Company.

0507. BRITISH BROADCASTING CORPORATION, Broadcasting Research Department, Portland Place, London W1A 1AA, England.

Project Title:
Evaluation of a Television Series "So You Want to Stop Smoking".

Principal Investigator:
Dyer, N.
Objective:
To (1) study attitudes toward smoking and smoking behavior among viewers and nonviewers before and after the first screening of the series; (2) study attitudes toward aspects of the series (presenter and information given); and (3) study attitudes toward the booklet offered in conjunction with the series.
Methods or Approach:
Three independent quota samples, designed to be representative of the population of the United Kingdom, were questioned. Two surveys were conducted before and one after the series was presented. A large sample of names and addresses of smokers was compiled from one of the broadcast company's continuous surveys. After the series, a questionnaire was sent enquiring whether or not the series had been watched and whether or not the respondent had given up smoking. Responses were sent to the BBC's viewing panel. A random sample of viewers who requested the booklet offered was also selected.
Results to Date:
Viewers were more likely than nonviewers to give up smoking. It was also found that the review panel generally thought highly of the series and the booklet was well received. However, the element of self-selection as viewers among smokers and those requesting booklets is clear. Data was analyzed by region, number of cigarettes smoked, age, sex, class, and desire to give up smoking.
Project Dates:
1981–1983.
Financial Support:
British Broadcasting Corporation; Health Education Council, London.

0508. BROMPTON HOSPITAL, MEDICAL RESEARCH COUNCIL, Tuberculosis and Chest Diseases Unit, Fulham Road, London SW3 6HP, England.

Project Title:
Assessment of the Carcinogenicity of Isoniazid in Patients with Pulmonary Tuberculosis.

Principal Investigators:
Stott, H.; Fox, W.N.; Peto, J.T., et al.
Objective:
To determine risk of lung cancer, leukemia, and cancer of the lymph nodes in tuberculosis patients given high doses of isoniazid.
Methods or Approach:
A followup is being conducted of nearly 4,000 adult tuberculous patients admitted to two hospitals from 1950 to 1957. Details of the dosage of isoniazid received by the patients (including the daily dosage and duration) have been recorded, as well as other antituberculosis drugs received, a crude estimate of exposure to ionizing radiation and of the smoking history in males. Deaths among the population are determined from the Office of Population Censuses and Surveys for England and Wales and the mortality in these patients is compared with that expected in the general population in England and Wales of the same age and sex occurring during the same period.
Results to Date:
Although there is no evidence of carcinogenic effect, a further 1,300 patients admitted to hospital between 1940 and 1949 are being studied to try to explain a decrease in cancer mortality for those patients starting treatment between 1950 and 1952. In view of the long induction time between first exposure to a carcinogen and the development of cancer, the study is being continued indefinitely.
Project Dates:
1965–continuing.
Financial Support:
MRC, United Kingdom (00233).

0509. CARDIOTHORACIC INSTITUTE AT MIDHURST, Midhurst, West Sussex, GU29 0BL, England.

Project Title:
Lung Function in West Sussex Firemen.

Principal Investigator:
Horsfield, K.
Objective:
To determine whether firemen in West Sussex suffer damage to lung resulting from occupational exposure to smoke.
Methods or Approach:
A randomly selected group of 101 fireman was followed for 4 years. Questionnaires on respiratory symptoms and smoking habits were completed, and lung function tests were conducted at 6-month intervals for 2 years, and annually for 2 years. Tests included lung volume, expiratory flows, dead space, and mixing efficiency. A group of 69 nonsmokers from other occupations served as controls.
Results to Date:
Data after 3 years show a similar rate of loss of forced expiratory volume in 1 sec (FEV_1) in the two groups, although mean absolute value of FEV_1 is higher in firemen. Ex-smokers had lowest mean value to start with, but overtook smokers at 1 to 2 years. Never smokers have the highest mean value. As a result of routine use of breathing apparatus, firemen do not seem to suffer occupational lung damage.
Project Dates:
November 1974–continuing.
Financial Support:
Colt Foundation.

0510. COOKRIDGE HOSPITAL, YORKSHIRE REGIONAL CANCER ORGANIZATION, Department of Epidemiology, Leeds LS16 6QB, West Yorkshire, England.

Project Title:
Epidemiology of Lymphomas and Leukaemias in the Yorkshire Region.

Principal Investigators:
Cartwright, R.A.; Bird, C.C.; Richards, I.P.D., et al.
Objective:
To conduct a prospective epidemiological investigation of all types of leukemia and lymphoma occurring within the Yorkshire region, including extrinsic and intrinsic etiological factors.
Methods or Approach:
In the case–control study, hospital controls are matched for sex and age with cases. All participants are interviewed using a standard questionnaire covering a wide range of topics of possible etiological significance, including smoking habits. Clinical and hematopathological evaluation is made of all cases.
Results to Date:
Data on smoking habits has not yet been analyzed.
Project Dates:
October 1979–December 1986.
Financial Support:
Leukaemia Research Fund, England.

0511. DARLINGTON MEMORIAL HOSPITAL, Darlington, County Durham, England.

Project Title:
Asthma Survey 1983.

Principal Investigator:
Connolly, C.K.
Objective:
To (1) assess control of reversible airway obstruction and development of fixed airway obstruction in subjects attending outpatient consultative clinics; (2) determine influence of age, duration of asthma, and social factors; and (3) analyze relationship between control and drug regimens.
Methods or Approach:
On the first visit in 1983, a brief questionnaire was completed for all patients. In addition to PFR and FEV_1, maximum PFR and FVC were assessed, where necessary, with a trial of steroids. Residence, presence of children and pets in the home, and occupation were noted. Smoking habits and atopic status were recorded. Social class was assessed by occupation. Where patients were not on satisfactory maintenance treatment, additional recordings were made for the first satisfactory visit (provided the visit was in 1983).

Results to Date:
Preliminary analysis suggests that age and duration of asthma determine development of fixed airway obstruction, particulary in atopic subjects and cigarette smokers. The effect of social class is complicated because, particularly with atopics, pulmonary function is initially decreased in lower social groups. Age is a more important factor in control of the reversible element of obstruction, which also deteriorates with increasing duration of asthma. Initial examination of social factors suggests that subjects in lower social classes and cigarette smokers have generally poorer performance than nonsmokers and those in higher social classes. Atopy is an additional unfavorable factor, as is absence of central heating in the patient's home.
Future Plans:
Following modifications based on earlier surveys, the project will be repeated in 1988.
Project Dates:
January 1983–December 1985.
Financial Support:
Darlington Memorial Hospital, England.

0512. FRIARAGE HOSPITAL, Northallerton, North Yorkshire DL6 1JG, England.

Project Title:
Diurnal Variations in Airway Obstruction.

Principal Investigator:
Connolly, C.K.
Objective:
To study diurnal rhythm in airway obstruction, particularly in asthmatic and bronchitic patients; determine whether the pattern of diurnal variation is different in persons who produce sputum (generally cigarette smokers).
Methods or Approach:
Subjects (500 normal asthmatics and bronchitics) will record peak flow rate over a period of 4 hours before and after bronchodilator for 7 days. History of atopy and sputum production will be noted. Sputum and blood eosinophil levels will be determined and skin tests to simple allergens will be made. Baseline spirometry will be by dry wedge spirometer. PFR will be fitted to a cosinar model and also analyzed by simple calculation of amplitude variation in morning and evening dip. Suitability of analyses will be assessed for different groups of subjects, depending on their history, eosinophil levels, atopic status, cigarette smoking, and clinical diagnosis. Other models will also be tried, in particular exponential recovery from a single event ("morning dip" happening in the early hours of the morning).
Results to Date:
Project is in a preliminary phase.
Project Dates:
July 1984–April 1986.
Financial Support:
Yorkshire Regional Health Authority.

0513. GUY'S HOSPITAL MEDICAL SCHOOL, Department of Anaesthetics, London Bridge, London SE1 9RT, England.

Project Title:
Influence of Smoking on Peri-Operative Morbidity.

Principal Investigator:
Jones, R.M.
Objective:
To identify factors that alter risk factors in smokers presenting for surgery.
Methods or Approach:
Pathophysiological changes associated with smoking and time-course of reversibility of such changes are reviewed.
Results to Date:
One day's abstinence provides a demonstrable increase in cardiovascular fitness, due to elimination of carbon monoxide and nicotine. Abstinence for 6 weeks allows some reversal of small airways narrowing, ciliary activity, and tracheobronchial clearance, leading to reduction in postoperative respiratory morbidity. Six weeks also allows some aspects of immune function to return to normal (e.g., pulmonary alveolar macrophage activity). Smokers have lower incidence of postoperative deep vein thrombosis than nonsmokers.
Future Plans:
Time course of reversibility of pathophysiological changes after smoking cessation will be further identified.
Project Dates:
1984–continuing.
Financial Support:
University of London.
References:
(1) Pearce, A.C.; Jones, R.M. "Smoking and Anesthesia: Preoperative Abstinence and Perioperative Morbidity." *Anesthesiology* 61:576-584, 1984. (2) Jones, R.M. "Smoking Before Surgery: The Case for Stopping." *British Medical Journal* (In press).

0514. HAMMERSMITH HOSPITAL, ROYAL POST-GRADUATE MEDICAL SCHOOL, Du Cane Road, London WL2 0HS, England.

Project Title:
Factors Influencing the Progression of Chronic Airway Disease in Male Smokers.

Principal Investigator:
Pride, N.B.
Objective:
To examine factors determining susceptibility for developing chronic airway narrowing among male smokers; assess methods for early detection of airway disease.
Methods or Approach:
Detailed questionnaires, chest radiographs, and tests of peripheral lung function will be applied sequentially to a group of 250 working men in West London. Smoking habits will be characterized by history, carbon monoxide in expired air, plasma cotinine, and butt analysis. Detailed smoking patterns will be completed in a subgroup. Capillary PO_2 and PCO_2, diffusing capacity, bronchial reactivity to inhaled histamine and beta agonists, blood eosinophilia and immunoglobulin E will also be measured. In subgroups, the effect of respiratory infection, live influenza vaccination, changes in smoking history, and α_1-antitrypsin status will be investigated.
Results to Date:
Findings to date have shown that acute respiratory infections have effects lasting a maximum of 8 weeks. Intermediate α_1-antitrypsin deficiency is only a weak risk factor. Increased bronchial reactivity is associated with accelerated decline in forced expiratory volume in 1 sec, while flow at the end of a maximum expiration and slope of the alveolar plateau appeared to be the most promising tests for detecting early changes. In young men, the predictive power of spirometry can be improved by correlation with tracheal size, but this relationship is weaker in middle-aged men.
Future Plans:
During planned long-term followup, tests will be developed to identify high-risk smokers.

Project Dates:
September 1974–continuing.
Financial Support:
MRC, United Kingdom; Chest, Heart and Stroke Association, United Kingdom; Tobacco Advisory Council, United Kingdom.

0515. HEALTH AND SAFETY EXECUTIVE, MDB3, Magdalen House, Trinity Road, Bootle, Merseyside, L20 3QZ, England.

Project Title:
Survey of U.K. Asbestos Workers.

Principal Investigators:
Jones, R.D.; Hodgson, J.T.
Objective:
To (1) study the mortality incidence of persons exposed to asbestos since the inception of the United Kingdom 1969 asbestos regulations; (2) study any relationship between chest x-ray findings, basal crepitations, clinical symptoms, and development of asbestos-related disease; and (3) study the effect of smoking on mortality pattern in general and on the development of asbestos-related disease in particular.
Methods or Approach:
All persons working in processes which are covered by the asbestos regulations are seen at 2-year intervals. A respiratory questionnaire is completed, smoking history and habit are noted, and the presence or absence of basal crepitations on clinical examination is recorded. A chest x ray is also carried out. The population under surveillance has been increased to include all workers covered by the Asbestos Licensing Regulations, 1983 (effective from January 1984). The regulations cover all asbestos insulators and strippers who are now subject to medical examination twice a year, which is identical to that carried out under the 1969 regulations.
Results to Date:
An interim mortality study covering the period 1971-1981 will be published in early 1985.
Future Plans:
The project is likely to be ongoing for a number of years.
Project Dates:
1974–continuing.
Financial Support:
Health and Safety Executive.

0516. HEREFORDSHIRE HEALTH AUTHORITY, Victoria House, Elgin Street, Hereford, Herefordshire, HR4 0AN, England.

Project Title:
Factors Influencing Teenage Smoking in Herefordshire.

Principal Investigators:
Brooks, P.E.; Goodger, B.M.
Objective:
To (1) assess attitudes and practices of shopkeepers in relation to the sale of cigarettes to children; (2) evaluate level of knowledge of shopkeepers on the law prohibiting such sales; (3) determine impact of campaigns directed toward shopkeepers to increase awareness of the law; (4) assess attitudes of youth club leaders on smoking in children; and (5) establish level of encouragement or discouragement of smoking in youth club environments.
Methods or Approach:
A market research agency will be employed to apply structured questionnaires in interviews with a sample of 100 to 200 cigarette sales outlets in the district. Semistructured interviews will be conducted with a sample of 10 youth club leaders.
Results to Date:
Project is in a preliminary phase.
Future Plans:
Based on findings, focus will be on problems of teenage smoking habits to provide relevant interventions.
Project Dates:
January 1985–March 1985.
Financial Support:
West Midlands Regional Health Authority.

0517. INSTITUTE FOR SOCIAL STUDIES IN MEDICAL CARE, 14 South Hill Park, London NW3, England.

Project Title:
Teenage Mothers and Smoking.

Principal Investigators:
Simms, M.; Smith, C.
Objective:
To determine the smoking habits of adolescent mothers in England and Wales.
Methods or Approach:
A national survey was conducted of 456 adolescent mothers in England and Wales.
Results to Date:
Adolescent mothers smoked much more heavily than adolescents as a whole. Smoking appeared to be associated with a number of problems or social disadvantages. Smoking was also associated with boredom. One-third of the women are trying to give up smoking. Social policy recommendations were made.
Project Dates:
1978–1984.
Financial Support:
United Kingdom Department of Health.
Reference:
Simms, M.; Smith, C. "Teenage Mothers and Smoking." *Health Education Journal* 42(3):87-89, 1983.

0518. INSTITUTE OF CANCER RESEARCH, Division of Epidemiology, Block D, Clifton Avenue, Sutton, Surrey SM2 5PX, England.

Project Title:
Smoking Behavior of Health Service Personnel.

Principal Investigators:
Chilvers, C.; Calnan, M.
Objective:
To ascertain whether National Health Service personnel in special cancer hospitals smoke less than those in general hospitals or in the general population; discover whether experience with the harmful effects of smoking-related disease exerts a stronger influence on smoking behavior than other forms of knowledge.
Methods or Approach:
A survey of smoking habits of National Health Service personnel in two cancer hospitals, a cancer research institute, and a general hospital was carried out using a self-completion questionnaire. General population data, available from the General Household Survey, was used for comparison. Phase 1 provided a sampling frame for Phase 2, an interview survey carried out in a random sample, stratified by smoking habit, within each organization.

Results to Date:
Project has been completed and results are being prepared for publication.
Project Dates:
April 1982–1983.
Financial Support:
Cancer Research Campaign, United Kingdom.

0519. INSTITUTE OF CANCER RESEARCH, Division of Epidemiology, 25 Cedar Road, Sutton SM2 5DG, England.

Project Title:
Gloucestershire Study.

Principal Investigators:
Lee, P.N.; Field, W.E.; Wicken, A.J.
Objective:
To (1) determine how a cohort of six hospitalized groups differed on factors recorded on a questionnaire concerning respiratory symptoms and residential, occupational, medical, and smoking histories; (2) determine within disorder groups how survival is related to the information originally recorded; (3) test how representative the survivors are of the living population in Gloucestershire; and (4) investigate changes in respiratory symptoms and smoking habits in the survivors and examine how the progression of the former is related to changes in the latter.
Methods or Approach:
From 1963 to 1967, information on respiratory symptoms, residential, occupational, and medical history, as well as full details of smoking habits were obtained from 2,377 people in hospitals in Gloucestershire. Those selected formed six groups: lung cancer, chronic bronchitis, other chest diseases, cardiac, orthopedic, and other cancer cases. Between 1974 and 1977, an attempt was made to reinterview those still alive, to determine their current smoking habits and respiratory symptoms, and to find the cause of death of those who had died.
Results to Date:
Results are not yet available.
Project Dates:
1963–continuing.
Financial Support:
Tobacco Advisory Council, England.

0520. INSTITUTE OF PSYCHIATRY, Departments of Neurology, Pharmacology, and Psychiatry, De Crespigny Park, London SE5 8AF, England.

Project Title:
Biochemical Studies of Brain Nicotinic Mechanisms.

Principal Investigators:
Jenner, P.G.; Reavill, C.; Stolerman, I.P.
Objective:
To further characterize binding of nicotinic ligands to brain tissue; investigate a possible second site involved in central nervous system effects of nicotine.
Methods or Approach:
Previous studies have used radiolabeled (±)-nicotine as the ligand. The generality of observations needs to be checked with labeled (-)-nicotine, corresponding to the naturally occurring substance. Binding studies for a possible second site will use labeled nicotinic antagonists (compounds that block behavioral effects of nicotine but do not inhibit nicotine binding and thus may act at another closely related site on a proposed nicotine receptor complex). The method for nicotine is based on published filtration procedures, using crude synaptosomes prepared from rat brains. Binding of labeled (-)-nicotine is determined over concentrations of 0.25 nmol to 125 nmol to define specific binding, with each concentration assayed in triplicate. Initially, since nicotinic antagonists have not previously been used as ligands, both centrifugation and filtration techniques will be employed.
Results to Date:
Preliminary results from nicotine binding assay confirm occurrence of 75 to 85 percent specific (i.e., nicotine-displaceable) binding. Scatchard plots show presence of a single high-affinity site. Inhibition experiments confirm that binding is stereoselective and that binding is potently inhibited by certain nicotine analogues (anabasine and cytisine).
Future Plans:
Characteristics and regional distribution of binding sites for nicotine and antagonists will be compared to determine whether such sites are identical. Information obtained will be used in behavioral experiments.
Project Dates:
October 1984–September 1985.
Financial Support:
AB Leo Foundation.

0521. INSTITUTE OF PSYCHIATRY, Departments of Pharmacology and Psychiatry, De Crespigny Park, London SE5 8AF, England.

Project Title:
Behavioural Pharmacology of Nicotine.

Principal Investigators:
Kumar, R.; Stolerman, I.P.
Objective:
To (1) investigate how certain behavioral effects of nicotine are centrally mediated through nicotinic receptors and other neurotransmitter systems; (2) determine whether central effects are mediated primarily through cholinergic mechanisms; (3) determine whether certain binding sites for nicotine, previously identified on rat brain membranes, are functional receptors; and (4) determine whether effects of microinjections of nicotine into brain regions can be related to regional distribution of nicotine binding sites.
Methods or Approach:
Behavioral measures include tests of drug discrimination and conditioned taste aversions, with responses to nicotine compared with those to certain analogues or after pretreatment with specific antagonists. Male hooded rats are used for all experiments. For studies on nicotine discriminative stimulus (cue), rats are trained to discriminate nicotine from saline in a standard, two-bar, operant conditioning procedure with food reinforcement. After performance reaches criterion, either generalization experiments with novel drugs or doses are carried out, or effects of pretreatment with nicotinic or other antagonists are studied. When necessary, trained rats are implanted with guide cannulae aimed at a lateral ventricle or a brain region. For studies of conditioned taste aversions, rats are injected with either nicotine or saline after brief periods of access to distinctively flavored but pharmacologically inactive solutions (saccharin or sodium chloride).
Results to Date:
The nicotinic-cholinergic analogues anabasine and cytisine are generalized in rats trained to discriminate a 0.1 mg/kg dose of nicotine. Nonnicotinic drugs are not generalized, confirming specificity of the nicotine cue. Mecamylamine produces a block of the nicotine cue that cannot be reversed by increases in nicotine dose. The correlation with characteristics of nicotine binding sites suggests that nicotine acts primarily through a

cholinergic receptor. Nicotine is also highly potent in producing conditioned taste aversions, suggesting that tobacco use may be regulated by both reinforcing and aversive drug effects. Nicotine injected into brain regions may be generalized with systemic nicotine. Neither dopamine nor 5-hydroxytryptamine antagonists blocked responses to nicotine.

Future Plans:
Investigations will include (1) localization of the origin of the nicotine cue to one or more brain regions; (2) determination of the discriminative effects of some nicotine metabolites; and (3) further characterizations of central nicotinic receptors by pretreatment studies with different types of antagonists, including chlorisondamine, which produced a long-term block when injected intraventricularly.

Project Dates:
January 1980–June 1985.

Financial Support:
MRC, England.

0522. INSTITUTE OF PSYCHIATRY, ADDICTION RESEARCH UNIT, 101 Denmark Hill, London SE5 8AF, England.

Project Title:
Psychological and Pharmacological Basis of Tobacco Dependence.

Principal Investigators:
Russell, M.A.H.; Jarvis, M.J.; West, R., et al.

Objective:
To (1) measure the pharmacokinetics of nicotine in humans after smoking and other forms of nicotine intake; (2) measure smoke intake and puffing patterns of smokers and response to different types of cigarettes; (3) assess exposure to passive smoking using biochemical markers of smoke intake; (4) study absorption from a solution of nicotine applied nasally and evaluate it as an aid to cessation; and (5) study the cigarette withdrawal syndrome.

Methods or Approach:
Measures of nicotine, cotinine, and carbon monoxide were applied to the study of active and passive smoking and to other forms of nicotine intake.

Results to Date:
Several studies have been completed and results have been published; other studies are in progress. Results indicate that smokers regulate smoke intake so that there is little correlation between nicotine delivery from cigarettes and blood levels of smokers; blood nicotine and cotinine levels are only slightly reduced in smokers of low-yield cigarettes compared with smokers of high-yield brands; measurement of cotinine in blood shows a dose–response relationship with passive smoke exposure; nicotine chewing gum alleviates severity of withdrawal symptoms when compared with placebo gum; and nasal nicotine solution provides an effective route of nicotine administration and shows promise as an aid in smoking cessation.

Project Dates:
October 1983–October 1988.

Financial Support:
MRC, United Kingdom.

References:
(1) Feyerabend, C.; Ings, R.M.J.; Russell, M.A.H. "Nicotine Pharmacokinetics and Its Application to Intake From Smoking." *British Journal of Clinical Pharmacology* (In press). (2) Russell, M.A.H.; Jarvis, M.J.; Iyer, R., et al. "Relation of Nicotine Yield of Cigarettes to Blood Nicotine Level of Smokers." *British Medical Journal* 280:972-976, 1980. (3) Russell, M.A.H.; Jarvis, M.J.; Feyerabend, C., et al. "Nasal Nicotine Solution: A Potential Aid to Giving Up Smoking?" *British Medical Journal* 286:683-684, 1983. (4) West, R.J.; Jarvis, M.J.; Russell, M.A.H., et al. "Effect of Nicotine Replacement on the Cigarette Withdrawal Syndrome." *British Journal of Addictions* 79:215-219, 1984. (5) Jarvis, M.J.; Tunstall-Pedoe, H.; Feyerabend, C., et al. "Biochemical Markers of Smoke Absorption and Self-Reported Exposure to Passive Smoking." *Journal of Epidemiology and Community Health* 38:335-339, 1984.

0523. KING'S COLLEGE SCHOOL OF MEDICINE AND DENTISTRY, Department of Community Medicine, Denmark Hill, London SE5 8RX, England.

Project Title:
Smoking in the Workplace: A Trade Union Approach.

Principal Investigators:
Lock, P.M.; McEwen, J.

Objective:
To explore how the resolution on smoking adopted by the Trades Union Congress in 1981 can be translated into acceptable and effective action in the workplace.

Methods or Approach:
Unions that have shown an interest in the problem of smoking have been approached and the resolution has been discussed with them. Information has been collected about views on smoking, health, and safety, and on ways of tackling the smoking issue that are compatible with a union ethos. With active participation of unions and cooperation of management, surveys have been conducted at two predominantly blue-collar sites to determine (1) whether action on smoking in the workplace is acceptable in principle; (2) views on specific types of activity (e.g., areas where smoking might be restricted, help for smokers who want to quit); and (3) knowledge of the effects of smoking and attitudes toward smoking.

Results to Date:
About 75 percent of respondents on both sites favor some form of action that would protect nonsmokers from smoke and encourage smokers to quit. This willingness to see something done translates into a variety of possible types of action, which indicates that care is needed when planning programs. Attitudes about smoking, even among confirmed smokers, indicate strong acceptance that smoking is not to be encouraged, and that it can be unpleasant to nonsmokers. However, there are strong views that smokers who wish to continue with the habit should be allowed to do so. Knowledge of the extent and type of ill health associated with smoking is variable; confirmed smokers either do not know or are unwilling to accept health evidence. Responses from smokers who want to quit are similar to those of ex-smokers and nonsmokers.

Future Plans:
In conjunction with other workplace projects, a *Good Practices Guide to Action on Smoking at Work* is being produced to bring together evidence supporting action on smoking in the workplace and examples of policies and programs, the criteria of successful action.

Project Dates:
October 1984–March 1985.

Financial Support:
Health Education Council of England and Wales.

0524. KINGSTON POLYTECHNIC, Penrhyn Road, Kingston, KT1 2EE, England.

Project Title:
Information That Affects Intention to Stop and Confidence in Quitting.

Principal Investigator:
East, J.R.
Objective:
To test effectiveness of different message formulations with different population segments, using intention and confidence as criteria.
Methods or Approach:
Earlier data indicate that intention predicts a cessation attempt, but that confidence is an independent determinant of success in quitting. It follows that persuasive communication should increase both intention and confidence to be effective. An experimental approach will be used to test the hypothesis.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–December 1986.
Financial Support:
Kingston Polytechnic.

0525. KINGSTON POLYTECHNIC, Health Education Research Team, Penrhyn Road, Kingston KT1 2EE, England.

Project Title:
Identifying Attitude Factors Associated With Smoking Cessation.

Principal Investigators:
Moreton, W.J.; East, J.R.
Objective:
To identify belief likelihoods and evaluations that are related to smoking abstinence and that are changeable.
Methods or Approach:
The likelihood and value of outcomes of giving up cigarettes were measured among smokers attending a cessation clinic. Measures were taken on first attendance and 3 and 6 weeks later. Abstinence period was measured 3 months later.
Results to Date:
Changes in smokers' beliefs about giving up smoking correlate with abstinence and relapse tendency (measured by beliefs about having "one cigarette" after giving up). Negative affect changes are associated with abstinence in both sexes, but changes in health beliefs are more often associated with abstinence among men. Abstinence in women was related to perceptions of what they thought others thought they should do; men seemed more dependent on personal gains from quitting, although personal gains were correlated with perceived social support. Results indicate that persuasive communications in mass media should emphasize social support to maximize influence on women, and personal advantage to produce the most effect among men. Mass media should also recognize the important part that other people play in maintenance of abstinence.
Future Plans:
Studies will examine relative impact of communications with different content on smoking intentions. Ancillary to the present study was development of software for designing appropriate questionnaires and analysis of data from studies utilizing the questionnaires.
Project Dates:
November 1978–1983.
Financial Support:
Kingston Polytechnic, England; Cancer Research Campaign, United Kingdom.

0526. KINGSTON POLYTECHNIC, Health Education Research Team, Penrhyn Road, Kingston KT1 2EE, England.

Project Title:
Industrial Smoking Cessation Schemes.

Principal Investigators:
Moreton, W.J.; East, J.R.
Objective:
To determine beliefs of employees and employers about smoking cessation schemes; identify acceptable ways of implementing smoking cessation in the workplace.
Methods or Approach:
Self-administered questionnaires are used in randomly selected large and small companies in the north and south of England. Groups sampled include employees, managers, union officials, and health staff. Questions deal with the payoffs of implementing health education in the workplace and the social influences on such a decision.
Results to Date:
Results are not yet available. Findings will be used in publications about smoking designed for different occupational roles in industry, which will be distributed by ASH (U.K.).
Project Dates:
January 1983–1985.
Financial Support:
Health Education Council, United Kingdom.

0527. LABORATORY OF THE GOVERNMENT CHEMIST, Department of Industry, Cornwall House, Stamford Street, London, SE1 9NQ, England.

Project Title:
Smoking and Health.

Principal Investigators:
Evans, W.H.; Darrall, K.G.
Objective:
To provide the Department of Health and Social Security and the Independent Scientific Committee on Smoking and Health with a regular list of tar, nicotine, and carbon monoxide yields of cigarettes on sale in the United Kingdom, published at approximately 6-month intervals in the form of league tables.
Methods or Approach:
Regular testing of approximately 140 major cigarette brands on sale in the U.K. for total particulate matter (Cambridge filter), water (GLC), nicotine alkaloids (cyanogen chloride), and carbon monoxide (NDIR), is undertaken on samples drawn at the point of manufacture or importation. The methods of analysis have generally been developed in conjunction with the U.K. tobacco industry and, where possible, these methods comply with current ISO standards.
Results to Date:
Since 1970, the sales-weighted average tar, carbon monoxide, and nicotine yields have continued to decline from 22 mg, 17 mg, and 1.4 mg, respectively, and by 1984 were 15 mg, 14 mg, and 1.3 mg, respectively. Tables of current yields are published every 6 months by the Department of Health and Social Security.
Future Plans:
The automated methods have been brought under microprocessor control and will be linked to the laboratory's in-house computer to increase the analytical capacity.

Project Dates:
1972–continuing.
Financial Support:
Department of Health and Social Security, United Kingdom.
Reference:
Fairweather, F.A.; Carmichael, I.A.; Phillips, G.F., et al. "Changes in the Tar, Nicotine, and Carbon Monoxide Yields of Cigarettes Sold in the United Kingdom." *Health Trends* 13(3):77-81, August 1981.

0528. LONDON HOSPITAL MEDICAL SCHOOL, Turner Street, London E12 AD, England.

Project Title:
Spitalfields Heart Disease Prevention Project.

Principal Investigators:
Silman, A.; Loysen, E.
Objective:
To determine whether adding a nurse to a general practice in an inner-city, multiracial area has any effect on ischemic heart disease risk factor prevention, with particular reference to smoking, weight, and blood pressure control.
Methods or Approach:
All patients on the general practice register between the ages of 35 and 65 were sent a letter inviting them to attend for screening to record blood pressure, smoking habits, weight, family history of heart disease, and urine test for sugar and protein. Intervention for smoking, conducted as necessary by the nurse, included interview, issue of leaflets, and a request to return at monthly intervals. In the second year of the program, the process will be repeated to determine whether risk factors have declined.
Results to Date:
Results are not yet available.
Project Dates:
September 1983–September 1985.
Financial Support:
North East Thames Region Award.

0529. LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, TUC CENTENARY INSTITUTE OF OCCUPATIONAL HEALTH, Keppel Street, London WC1E 7HT, England.

Project Title:
The Mortality of Cadmium Workers.

Principal Investigators:
Kazantzis, G.; Armstrong, B.G.; Ades, A.
Objective:
To determine the mortality pattern of persons occupationally exposed to cadmium and its compounds, with particular reference to lung and prostatic cancer, hypertension, cerebrovascular disease, bronchitis, emphysema, nephritis, and nephrosis.
Methods or Approach:
The study cohort comprises men born before 1940 and exposed to cadmium for more than 1 year between 1940 and 1970 who were followed up to the end of 1984. Case–control sets were selected from within the cohort for further study of deaths due to prostatic and renal cancer, lung cancer, bronchitis, emphysema, nephritis, and nephrosis. Data on smoking habits has been collected and added to computer file.
Results to Date:
A statistically significant excess of deaths due to bronchitis showed a strong relationship with duration and intensity of exposure to cadmium. There was statistically significant excess mortality due to lung cancer in men employed more than 10 years in the lowest exposure category that is unlikely to be related to cadmium exposure. No excess mortality was found for prostatic cancer, cerebrovescular disease, or renal disease.
Future Plans:
A prospective cohort study of cadmium workers will be conducted, and lung cancer mortality will be investigated further by case–control analysis.
Project Dates:
1979–1989.
Financial Support:
International Lead Zinc Research Organisation.

0530. LONDON UNIVERSITY, INSTITUTE OF PSYCHIATRY, Denmark Hill, London, England.

Project Title:
Individual Differences in Psychophysiology of Smoking and Smoking Behavior.

Principal Investigator:
O'Connor, K.P.
Objective:
To examine effect of smoking on individual differences in cortical slow potentials and performance under conditions of skilled and unskilled and stressful and nonstressful motor task performance.
Methods or Approach:
Surface recorded EEG and EMG motor potentials were measured in association with performance on a range of motor tasks involving different degrees of attention and physical effort. Groups of smokers were preselected according to situational smoking topology and personality score.
Results to Date:
In general, motor performance in all groups improved after smoking. Smoking affected parameters related to muscular effort in extroverts and motor skill in introverts. Smoking style also varied within groups according to motor set.
Project Dates:
September 1980–September 1986.
Financial Support:
American Tobacco Manufacturers Research Fund.

0531. MANCHESTER REGIONAL COMMITTEE FOR CANCER EDUCATION, Kinnaird Road, Manchester M2O 9QL, England.

Project Title:
Survey of Smoking Habits and Attitudes in Schools and Colleges in Northern England. Phase 2: Evaluation of Teaching Materials.

Principal Investigator:
Charlton, A.
Objective:
To identify patterns and background factors that might be used as guidelines for planning intervention materials for young people aged 9 to 19; evaluate effectiveness of materials.
Methods or Approach:
Phase 1 was by anonymous questionnaires administered to intact classes in entire schools. Phase 2 consists of pretests and posttests. In each of the three age groups (9-, 12-, and 16-year-olds), three groups have been randomly selected: (1) experimental group that is pretested, taught the lessons, and posttested 3 months later; (2) control group involved in pre- and posttesting only; and (3) control group with posttesting only. The pre- and posttesting is carried out by anonymous

questionnaire. Birthdates and other features are used for matching.

Results to Date:

Phase 1 found that there were three critical stages: (1) at 9 years of age, most children tried their first cigarette; (2) at 12 years of age there was an increase in the establishment of regular smoking; and (3) at 16 years of age, many of the smokers wanted to stop. Results also showed that (1) parents' opinions had a considerable influence on the child's decision to smoke; (2) the appearance of smoking is most important with younger children, but older ones support the idea that people smoke for confidence, to calm nerves, and for weight control; and (3) more girls than boys in the midteen years are smokers. Phase 2 is in a preliminary stage.

Project Dates:

April 1982–March 1985.

Financial Support:

Cancer Research Campaign, United Kingdom.

0532. MANCHESTER REGIONAL COMMITTEE FOR CANCER EDUCATION, Kinnaird Road, Manchester M2O 9QL, England.

Project Title:

Comparative Evaluation of "Quest" and "Assegai," Two Cancer Education Packages.

Principal Investigators:

Charlton, A.; Cribb, A.

Objective:

To assess the cognitive, affective, and behavioral changes (including smoking) following use of Quest and Assegai in teaching 16-year-olds about cancer in comprehensive and independent schools and in colleges of further education (vocational colleges).

Methods or Approach:

In each of the three types of educational institution, the following matched groups are participating: (1) experimental group, taught Quest and pre- and posttested by questionnaire; (2) similar experimental group taught Assegai; (3) control group pre- and posttested; and (4) control group posttested only. Each group is posttested three times, with a new control group added each time. Discussions with teachers are also being used.

Results to Date:

Project is in a preliminary phase.

Project Dates:

October 1982–September 1985.

Financial Support:

Cancer Research Campaign, United Kingdom.

0533. MEDICAL COLLEGE OF ST. BARTHOLOMEW'S HOSPITAL, Department of Environmental and Preventive Medicine, Charterhouse Square, London, EC1M 6BQ, England.

Project Title:

Biochemical Effects of Reducing the Tar Yield of Cigarettes.

Principal Investigators:

Wald, N.J.; Semmence, A.; Stephen, A.M., et al.

Objective:

To determine extent to which smokers switching to low-tar cigarettes inhale more smoke to compensate for lower tar yield.

Methods or Approach:

Participants in the randomized controlled trial must smoke at least five cigarettes/day ($\geq$ 16 mg tar/cigarette). Initially, all participants will switch to a brand containing 10 percent less tar. After 2 months, subjects will be randomized into three groups: (1) group A, no change; (2) group B, 40 percent less tar; or (3) group C, 10 percent less tar every 2 months. All subjects will be seen every 2 months for 10 months. At each visit, blood, urine, and breath samples will be collected. Blood and urine will be analyzed for cotinine by radioimmunoassay, and blood carboxyhemoglobin levels and breath carbon monoxide levels will be determined.

Results to Date:

Project is in a preliminary phase.

Project Dates:

June 1983–June 1986.

Financial Support:

Tobacco Products Research Trust; Independent Scientific Committee on Smoking and Health.

0534. MEDICAL COLLEGE OF ST. BARTHOLOMEW'S HOSPITAL, Department of Environmental and Preventive Medicine, Charterhouse Square, London EC1M 6BQ, England.

Project Title:

The BUPA Study.

Principal Investigators:

Wald, N.J.; Bailey, A.

Objective:

To investigate tobacco smoking as a risk factor for coronary heart disease (CHD) and cancer.

Methods or Approach:

Carboxyhemoglobin was measured and serum and urine samples collected and stored from the 22,000 men who were recruited for the study. Followup is by notification of death or cancer (656 to date) from the National Health Service Central Register. COHb levels and carbon monoxide (CO) yield of cigarettes smoked are used as index of cigarette smoke absorption. Extent of inhaling is adjusted to achieve similar intakes of nicotine/CO regardless of nicotine/CO yield of cigarette.

Results to Date:

Inhalation increases as tar yield decreases, but not sufficiently to achieve similar tar intake. Serum and urinary cotinine were higher in pipe smokers than in cigarette smokers, suggesting higher systemic nicotine levels. Since pipe smokers have little excess risk of CHD, higher chronic nicotine exposure is unlikely to be the cause of the excess seen in cigarette smokers.

Project Dates:

1975–continuing.

Financial Support:

MRC, United Kingdom; Imperial Cancer Research Fund.

0535. MIDDLESEX HOSPITAL MEDICAL SCHOOL, BLAND-SUTTON INSTITUTE, Mortimer Street, London W1P 7PP, England.

Project Title:

The Effects of Cigarette Smoke and Its Metabolites on Arterial Endothelium (Both In Vivo and In Vitro) and on Platelet Endothelial Interactions.

Principal Investigators:

Woolf, N.; Pittilo, R.M.

Objective:

To (1) determine whether exposure of small animals to smoke is followed by morphological alterations of the arterial endothelium; (2) investigate mechanisms responsible for any such alterations; and (30 assess effects of smoke on platelet–vessel wall interaction in the intact animal and in other systems.

Methods or Approach:
Rats are exposed to graded doses of fresh cigarette smoke. Exposure is followed by perfusion of the whole animal and ultrastructural studies of the aorta, employing both scanning and transmission electron microscopy. Platelet reactivity following smoking is assessed by phasing whole blood (obtained from human volunteers before and after smoking) across intact segments of rabbit aorta. Portions of aorta are examined by scanning electron microscopy and platelet adhesion is qualified. Cultured mesothelial and endothelial cells are exposed for set periods and human plasma taken before and after smoking. Endothelial cells are examined by scanning electron microscopy for evidence of morphological alterations.
Results to Date:
Exposure of animals to fresh cigarette smoke results in production of endothelial cell changes consisting of cell contraction and bleb formation. In all animals examined, microthrombi have been found in relation to the intact endothelium in low wall sheer rate areas just proximal to intercostal arteries. In humans, smoking medium-tar cigarettes resulted in a highly significant increase in the number of platelets adhering to undamaged rabbit aorta. Cultures of both mesothelial and endothelial cells show striking surface membrane changes consisting largely of blebs following exposure to post-smoking plasma.
Future Plans:
Studies will include effects on the in vivo model using filters that block either the vapor or particulate phase of smoke and cell culture and other chamber studies will be continued to identify mechanisms responsible for alterations already noted.
Project Dates:
January 1981–continuing.
Financial Support:
British Tobacco Industry.

0536. MIDDLESEX HOSPITAL, BLAND-SUTTON INSTITUTE OF PATHOLOGY, Mortimer Street, London W1P 7PP, England.

Project Title:
Cigarette Smoke Induced Cytotoxicity of Cultured Mesothelial Cells and Endothelial Cells.

Principal Investigators:
Pittilo, R.M.; Woolf, N.; Bull, H.A., et al.
Objective:
To examine effects of plasma obtained from human volunteers on cultured cells; investigate whether plasma obtained after cigarette smoking is more toxic to mesothelial cells than plasma obtained from blood collected before smoking.
Methods or Approach:
Plasma prepared from presmoking and postsmoking blood samples is placed in separate dishes of cultured cells for 30 minutes. Plasma is removed and cells covered with fresh media. Cells are examined by scanning electron microscopy (SEM) at varying times after treatment.
Results to Date:
Plasma obtained from normally nonsmoking volunteers after cigarette smoking is toxic to cultured mesothelial cells. Blebbing of the cells and rounding up of the cells is apparent on SEM analysis. Presmoking plasma samples had little effect on ultrastructure of cells.
Future Plans:
The effect of postsmoking samples on prostacyclin production by cells will be investigated.
Project Dates:
January 1984–December 1985.
Financial Support:
Bland-Sutton Institute of Pathology.

0537. MIDDLESEX HOSPITAL, BLAND-SUTTON INSTITUTE OF PATHOLOGY, Mortimer Street, London W1P 7PP, England.

Project Title:
Effects of Nicotine on the Ultrastructure of Rat Thoracic Aorta and Its Ability to Produce Prostacyclin.

Principal Investigators:
Pittilo, R.M.; Bull, H.A.; Blow, C.M., et al.
Objective:
To establish whether nicotine is capable of producing endothelial cell damage; determine whether nicotine affects ability to produce prostacyclin.
Methods or Approach:
Nicotine was administered to rats as single injections and as a continuous infusion over a week. Thoracic aortas of the animals were examined by scanning electron microscopy to detect endothelial cell damage, and prostacyclin production was measured by radioimmunoassay.
Results to Date:
Nicotine administered as a single injection had no significant effect either on endothelial cell morphology or prostacyclin production. However, after chronic nicotine infusion, there was a moderate degree of endothelial cell damage, and a highly significant decrease in prostacyclin production.
Future Plans:
Effects of nicotine on cultured endothelial cell morphology and ability to produce prostacyclin will be examined.
Project Dates:
January 1981–December 1985.
Financial Support:
Bland-Sutton Institute of Pathology.

0538. MIDDLESEX HOSPITAL, Mortimer Street, London W1P 7PP, England.

Project Title:
Effects of Cigarette Smoking on Platelet Adhesion.

Principal Investigators:
Pittilo, R.M.; Woolf, N.; Machin, S.J., et al.
Objective:
To investigate interactions between platelets and endothelial cells following cigarette smoking.
Methods or Approach:
Blood, obtained from human volunteers before and after cigarette smoking, was passed over an intact endothelial surface (rabbit aorta placed on the central spear of a Baumgartner chamber). Endothelial surfaces were examined after 10 minutes exposure to pre- and postsmoking blood using scanning electron microscopy. Platelet aggregation and FVIIIG) level studies were also carried out.
Results to Date:
A significant increase in platelet adhesion to the endothelial surface was evident with postsmoking blood compared with presmoking blood. FVIIIG) levels were higher in the majority of postsmoking samples than in presmoking samples. No difference in platelet aggregation was detected when normally nonsmoking volunteers were used.
Future Plans:
Studies will use blood obtained from volunteers who are regular smokers and from nonsmokers before and after exposure to a smoke-laden environment.

Project Dates:
January 1983–December 1985.
Financial Support:
Middlesex Hospital, England.

0539. MINISTRY OF DEFENCE, Ministry of Defence Army, First Avenue House, High Holborn, London WC1V 6HE, England.

Project Title:
Smoking Habits of Young Soldiers.

Principal Investigators:
Crowdy, J.P.; Oelman, B.J.; Lewthwaite, C.J.
Objective:
To (1) investigate the smoking habits of young soldiers; (2) assess trends in these habits over time; (3) compare the habits and trends of successive cohorts of soldiers; and (4) investigate the relationships between smoking habits and morbidity.
Methods or Approach:
The smoking habits of three cohorts of 15- to 18-year-old entrants to the Army were ascertained from questionnaires. The cohorts were followed up at 5-year intervals to determine changes in smoking habits over time. The three cohorts were soldiers joining the Army in 1959, 1966, and 1971. Morbidity data on all the personnel have been collected while they remained in the Army. The relationship between smoking habits and morbidity are being studied.
Results to Date:
Young soldiers tend to smoke more heavily, and a greater percentage smoke than would be expected in a similarly aged group from the general population. In succeeding cohorts, smaller percentages smoked, and have smoked less heavily. Smoking habits were generally determined before entry to the Army, with the majority of regular smokers starting before the age of 17. There is an apparent trend for smoking to start at an earlier age.
Future Plans:
Morbidity data have now been collected for the first cohort for over 20 years, 15 years for the second, and 10 years for the third. Data for the analysis of the relationships between smoking habits and morbidity are now available.
Project Dates:
1959–1982.
Financial Support:
Ministry of Defence.

0540. MOUNT VERNON HOSPITAL, REGIONAL RADIOTHERAPY CENTRE, Marie Curie Research Wing for Oncology, Northwood, Middlesex HA6 2RN, England.

Project Title:
Second Primaries Possibly Associated With Cigarette Smoking.

Principal Investigators:
Dische, S.; Saunders, M.; Bennett, M.H.
Objective:
To investigate second primaries possibly associated with cigarette smoking in patients with bladder cancer.
Methods or Approach:
Patients with bladder cancer submitted to clinical trials using methods to sensitize hypoxic cells to radiation have been subjected to very careful followup.
Results to Date:
Of the males, 96 percent have a history of cigarette smoking. Carcinoma of the bronchus has been the most frequent cause of death other than carcinoma of the bladder.
Project Dates:
January 1966–1986.
Financial Support:
MRC, United Kingdom.

0541. MRC, EPIDEMIOLOGY AND MEDICAL CARE UNIT, Northwick Park Hospital, Watford Road, Harrow, Middlesex HA1 3UJ, England.

Project Title:
Northwick Park Heart Study.

Principal Investigator:
Meade, T.W.
Objective:
To study hemostatic variables that may be involved in the pathogenesis of occlusive vascular disease.
Methods or Approach:
A total of about 3,500 men and women in industrial groups in northwest London have been examined and are now being followed up. Blood was collected for estimations of fibrinolytic, platelet, and clotting factor activity, in addition to serum lipids.
Results to Date:
High levels of Factor VII, Factor VIII, and fibrinogen are each independently associated with an increased risk of subsequent cardiovascular death. The general epidemiology of these clotting factors is consistent with the hypothesis that they are causally involved in the onset of vascular disease. In particular, cigarette smokers have higher plasma fibrinogen levels than nonsmokers.
Project Dates:
April 1972–1984.
Financial Support:
MRC, United Kingdom; U.K. Department of Health and Social Security.

0542. MRC, EPIDEMIOLOGY AND MEDICAL CARE UNIT, Northwick Park Hospital, Harrow, Middlesex HA1 3UJ, England.

Project Title:
Social Class Smoking in the United Kingdom.

Principal Investigator:
Townsend, J.
Objective:
To investigate the response of different social classes to changes in the cigarette tax and health publicity.
Methods or Approach:
Cigarette consumption since 1958 is being analyzed for five social classes using a multiple regression analysis technique.
Results to Date:
Project is in a preliminary phase.
Project Dates:
1981–1983.
Financial Support:
MRC, United Kingdom.

0543. MRC, EPIDEMIOLOGY AND MEDICAL CARE UNIT, Northwick Park Hospital, Watford Road, Harrow, Middlesex HA1 3UJ, England.

Project Title:
Morbidity and Health Service Usage of Smokers.

Principal Investigator:
Townsend, J.
Objective:
To investigate the incidence of acute and chronic illness in terms of smoking experience, age, and social class; relate such information to health service use and work absenteeism.
Methods or Approach:
Analysis will be based on data from the National General Household Survey.
Results to Date:
Project is in a preliminary phase.
Project Dates:
1981–1983.
Financial Support:
MRC, United Kingdom.

0544. NEW ADDENBROOKE'S HOSPITAL, Department of Respiratory Physiology, Chest Clinic, Hills Road, Cambridge CB3 8RE, England.

Project Title:
Interactions Between Cigarette Smoke and Pulmonary Surfactant

Principal Investigators:
Cracknell, N.G.; Harmes, K.; Higenbottam, T.W., et al.
Objective:
To determine the role of surfactant in smoking-related diseases of the lung.
Methods or Approach:
Pressure volume loops are recorded from excised rat lungs that have been exposed either to whole smoke or to individual constituents of tobacco smoke. Surface tension properties of surfactant are recorded in vitro, on a surface balance before and after exposure to tobacco smoke or its constituents. Phospholipid analysis is performed on human brochoalveolar lavage specimens from smoking and nonsmoking patients.
Results to Date:
Whole smoke produced a change in pressure volume curves of isolated rat lungs, which had higher opening pressures and higher volumes on deflation. Whole smoke, but not gas phase, reduced hysteresis of surfactant recorded on surface balance. In human bronchoalveolar lavage fluid, no qualitative difference between phospholipids of smokers and nonsmokers was found.
Future Plans:
An isolated lung technique will be developed to look at individual constituents of tobacco smoke and effects of constituents on surfactant on surface balance. Quantitative analysis of phospholipids and enzymes in bronchoalveolar lavage specimens from smokers and nonsmokers will be conducted.
Project Dates:
September 1984–December 1985.

0545. NORTH DEVON DISTRICT HOSPITAL, Barnstaple, Devon EX31 4JB, England.

Project Title:
Validation of Smoking in Pregnancy.

Principal Investigator:
McGarry, J.
Objective:
To determine whether patients tell the truth about smoking habits by measuring breath carbon monoxide (CO).
Methods or Approach:
At each prenatal visit, breath CO is measured on all patients suspected of being smokers.
Results to Date:
Patients who say they smoke 1 to 5 cigarettes/day tell the truth. Patients who smoke more than 5 cigarettes/day underestimate smoking by 50 percent.
Future Plans:
Patients will be confronted with the information about smoking to determine whether they are likely to reduce consumption during pregnancy.
Project Dates:
1982–1987.
Financial Support:
Northeast Foundation, Exeter.

0546. NORTHWICK PARK HOSPITAL, Epidemiology and Medical Unit, Watford Road, Harrow, Middlesex HA1 36J, London, England. ST. MARY'S HOSPITAL MEDICAL SCHOOL, Department of General Practice, London, England.

Project Title:
The Relationship Between Secretor Status and Pulmonary Function in Smokers and Nonsmokers.

Principal Investigators:
Haines, A.P.; Cole, P.
Objective:
To determine whether nonsecretors of ABH antigens have poorer pulmonary function than secretors; examine whether the difference is greater in smokers than in nonsmokers.
Methods or Approach:
The possibility is being investigated among unselected patients (aged 17 to 70 years) registered with a general practitioner at a neighborhood health center in northwest London. Throat and mouth swabs are taken to determine whether carriage of *Hemophilus influenzae* is related to cigarette smoking and secretor status. The relationship between urinary cotinine and smoking history is also being examined in this population. Currently, about 1,300 individuals have attended for spirometry, standard interview, and testing for ABH secretor status. Breath carbon monoxide levels are being measured in addition to urinary cotinine, and routine biochemical and hematological tests are performed.
Results to Date:
Results for the first 1,000 participants do not suggest any significant differences in pulmonary function between secretors and nonsecretors of ABH antigens, either in smokers or in nonsmokers. Data analysis will continue.
Project Dates:
May 1983–August 1985.
Financial Support:
Northwest Thames Regional Health Authority.

0547. RADCLIFFE INFIRMARY, Department of Cardiovascular Medicine, ISIS, Oxford OX2 6HE, England.

Project Title:
Second International Study of Infarct Survival (ISIS-2).

Principal Investigators:
Collins, R.; Peto, R.; Sleight, P.
Objective:
To conduct a multicenter, randomized, placebo-controlled study of the effects of intravenous streptokinase (SK) and of oral aspirin on mortality after acute myocardial infarction (MI); conduct a case–control study of the causes of MI.

Methods or Approach:
A particular aim will be to determine whether different types of cigarettes (e.g., with different tar or nicotine yields) are importantly different in terms of MI survival. The exact relevance of particular types of food and drink (and other factors) will also be assessed. It is planned that some 20,000 to 30,000 patients admitted to hospitals within 24 hours of the onset of a suspected MI will be entered into the ISIS-2 randomized controlled trial. On admission, a 10 mL blood sample will be taken into a tube containing potassium EDTA and aprotinin and sent to a central laboratory for removal and storage of the plasma. After resolution of the initial crisis, a self-administered questionnaire may be completed by each patient to determine personal habits (smoking, drinking, eating, exercising). Comparison will be made with a similar blood sample and questionnaire from an age- and sex-matched member of the patient's family who has not suffered an MI. The case-control study should, because of the unusual size of ISIS-2, yield far more reliable evidence on risk factors than currently exists.
Results to Date:
Over 500 hospitals in Australia, Belgium, Canada, Denmark, Eire, Finland, France, Germany, Norway, Sweden, the United Kingdom, and the United States have agreed to collaborate in ISIS-2.
Future Plans:
Further trials of treatment of acute MI are planned in which blood samples and epidemiology questionnaires will be used.
Project Dates:
March 1985–December 1986.
Financial Support:
Behringwerke.

0548. RADCLIFFE INFIRMARY, Department of Community Medicine and General Practice, Gibson Building, Oxford OX2 6HE, England.

Project Title:
A Randomized Controlled Trial of the Effectiveness of Anti-Smoking Interventions by Nurses in General Practice.

Principal Investigators:
Sanders, D.J.; Fowler, G.; Marzillier, J.
Objective:
To (1) investigate the value of antismoking advice given by practice nurses to patients recruited during office visits; (2) evaluate effectiveness of demonstration of expired air carbon monoxide as an educational tool; (3) determine which smokers, in terms of socioeconomic group and smoking habit, are affected; and (4) validate claimed smoking cessation by urinary cotinine measurement.
Methods or Approach:
Approximately 1,500 smokers attending general practices in the Oxford region will be randomly allocated to three groups: (1) control group (nonintervention, to measure natural cessation rates); (2) advice group receiving a brief "health check" by the practice nurse, including advice and a leaflet about smoking cessation; and (3) advice group who receive a demonstration of level of carbon monoxide in their expired air in addition to advice and leaflet. All groups will be followed up at 1 month and 1 year. A sample of those who claim to have stopped smoking at 1-year followup will be asked for a urine sample and cotinine will be measured to validate cessation. A preliminary survey is being conducted to assess current activities and beliefs about smoking education among nurses. Content of advice to be delivered is being carefully planned and the need for additional health education training for nurses is being assessed.
Results to Date:
Project is in a preliminary phase.
Project Dates:
September 1984–September 1987.
Financial Support:
British Heart Foundation; Health Education Council, United Kingdom.

0549. ROYAL COLLEGE OF GENERAL PRACTITIONERS, Manchester Research Unit, 8 Barlow Moor Road, Didsbury, Manchester M20 OTR, England.

Project Title:
Royal College of General Practitioners' Oral Contraception Study.

Principal Investigator:
Kay, C.R.
Objective:
To evaluate the effects of oral contraceptives on health.
Methods or Approach:
The study is a continuing, long-term, prospective survey of approximately 46,000 women of childbearing age in the U.K. About 23,000 current oral contraceptive (OC) users and 23,000 patients who had never used OCs were recruited over a 14-month period for observation by 1,400 general practitioners throughout the U.K. All subjects were married, or living as married. A record of total reported morbidity and other relevant data is collected from the participating doctors every 6 months from each subject's respective date of recruitment to the study. The data are monitored by computer, and before analysis, are standardized for age, parity, social class, and cigarette consumption (at the time of recruitment). Morbidity is measured by calculating the first presentation only of each morbidity category and is related to the appropriate period of observation and expressed as rates per thousand woman years. All events occurring in pregnancy and the puerperium, together with associated periods of observation, are excluded from the calculations. An appropriate statistical test is then applied to comparisons of morbidity data in the user, ex-user, and control groups. Morbidity in relation to cigarette smoking is one of several parameters analyzed.
Results to Date:
The total mortality rate in women who had ever used OCs was increased by 40 percent, due to an increase in deaths from circulatory diseases of 1/5,000 uses per year. The excess mortality was almost exclusively confined to oral contraceptive users over the age of 35 years who smoked cigarettes and was related to the progestogen content of the combined oral contraceptives.
Future Plans:
Observations and analyses are expected to continue until 1988.
Project Dates:
May 1968–1988.
Financial Support:
MRC, United Kingdom.

0550. ROYAL FREE HOSPITAL, Department of Medical Physics and Thoracic Medicine, London NW3 2QG, England.

Project Title:
Effect of Smoking Cessation on Lung Clearance by Mucociliary Transport and Cough in Chronic Bronchitis.

Principal Investigators:
Agnew, J.E.; Pavia, D.; Clarke, S.W.
Objective:
To (1) study clearance of inhaled polystyrene particles from conducting airways in patients with chronic bronchitis; (2) compare rates of clearance in ex-smokers with rates in current smokers; and (3) quantitate relationship between sputum production and tracheobronchial clearance.
Methods or Approach:
Monodisperse ^{99}Tc^{m} 5-micron diameter polystyrene particles are inhaled under carefully controlled conditions. Scintillation counters placed anterior and posterior to the chest are used to monitor clearance from the lungs for 6 hours following inhalation with followup readings at 24 hours and (in some cases) 48 hours to estimate alveolar deposition.
Results to Date:
When clearance tests are matched for penetration of test particles and for sputum production, ex-smoking chronic bronchitics do not clear significantly faster than chronic bronchitics currently smoking. Clearance is faster in patients producing high sputum volumes than in those producing low sputum volumes. If smoking cessation in a particular patient leads to diminished sputum production, mucus clearance may worsen.
Future Plans:
Further analysis of data is to be carried out relative to the importance of depth of test particle lung penetration and of lung function.
Project Dates:
December 1979–continuing.
Financial Support:
Royal Free Hospital.
Reference:
Agnew, J.E.; Little, F.; Pavia, D., et al. "Mucus Clearance From the Airways in Chronic Bronchitis–Smokers and Ex-Smokers." *Bulletin Europeen de Physiopathologie Respiratoire* 18:473-484, 1982.

0551. ROYAL FREE HOSPITAL, Departments of Medical Physics and Thoracic Medicine, London NW3 2QG, England.

Project Title:
Effect of Cigarette Smoking on Radioaerosol Particle Deposition and Clearance.

Principal Investigators:
Agnew, J.E.; Pavia, D.; Clarke, S.W.
Objective:
To study deposition and clearance of inhaled radioactive polystyrene particles in healthy nonsmokers and in asymptomatic smokers.
Methods or Approach:
Monodisperse ^{99}Tc^{m} 5-micron diameter polystyrene particles are inhaled in a series of 450 mL breaths at mean flow rates of 20-50 L/min. Scintillation counters placed anterior and posterior to the chest are used to monitor clearance from the lungs for 6 hours following inhalation. A further reading at 24 hours post inhalation is used to estimate alveolar deposition. A gamma camera view 10 to 20 minutes post inhalation is used to assess penetration index (ratio of outer to inner zone ^{99}Tc^{m} radioactivity divided by the same ratio for inhaled ^{81}Kr^{m} gas). In some subjects, regional clearance is assessed from sequential gamma camera views.
Results to Date:
Under the same conditions of inhalation, little or no difference of penetration index occurs between smokers and nonsmokers, but alveolar deposition is lower in smokers than in nonsmokers. Using a regional analysis model to allow for regional values of alveolar deposition, preliminary results suggest that little or no impairment of particle clearances occurs in peripheral airways of asymptomatic smokers.
Future Plans:
Further applications of the regional clearance model are planned for comparing data from smokers with nonsmokers.
Project Dates:
1979–continuing.
Financial Support:
Royal Free Hospital, England.
References:
(1) Agnew, J.E.; Bateman, J.R.M.; Pavia, D., et al. "Radionuclide Demonstration of Ventilatory Abnormalities in Mild Asthma." *Clinical Science* 66:525-531, 1984. (2) Agnew, J.E.; Bateman, J.R.M.; Pavia, D., et al. "A Model for Assessing Bronchial Mucus Transport." *Journal of Nuclear Medicine* 24:170-176, 1984.

0552. ST. BARTHOLOMEW'S HOSPITAL, Anaesthetic Research Laboratory, West Smithfield, London EC1A 7BE, England.

Project Title:
Tobacco Smoke Inhalation and Smoking Habits, Motives and Attitudes.

Principal Investigators:
Saloojee, Y.; Cole, P.V.
Objective:
To relate inhalation habits of smokers to reasons given for smoking; investigate differences between smokers and ex-smokers in relation to factors that contribute to continued smoking or abstention.
Methods or Approach:
An objective measure of tobacco smoke inhalation was included in a survey of self-reported smoking habits, motives, attitudes, and efforts to stop in a normal population. Smoke intake was quantified by measuring carbon monoxide (CO) in expired air; motives were assessed with the "reasons for smoking questionnaire" (Russell et al. 1974). When necessary, ex-smokers were asked to answer questions retrospectively.
Results to Date:
Factor analysis showed that distinctive patterns of motivation to smoke exist and that the "composite model of smoking" is replicable. Both expired air CO levels and cigarette consumption are positively correlated with stimulation and addictive and automatic types of smoking. Ex-smokers differed significantly from current smokers on a number of measures of dependency on tobacco; social or psychological explanations for smoking in the past were common.
Project Dates:
January 1982–December 1984.
Financial Support:
Cancer Research Campaign, United Kingdom.

0553. ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Department of Psychology, Cranmer Terrace, London SW17 0RE, England.

Project Title:
Helping People Stop Smoking. Support Services in the UK.

Principal Investigators:
Raw, M.; Heller, J.
Objective:
To (1) describe development of support services in the United

Kingdom to help people stop smoking; (2) report distribution, staffing, funding, recruitment procedures, treatment methods, and effectiveness; (3) discuss role of support services and health professionals in smoking cessation; and (4) prepare recommendations for action at district and national levels.

Methods or Approach:

From 1981 to 1983, all known smokers' clinics in the United Kingdom were surveyed (mail questionnaire and some visits) to determine how many were still operating, where they were located, who ran the clinic, what methods were used, and how successful the programs were. At least one example of each type of clinic was selected for a visit. Cooperative help was provided to some clinics for long-term followup of clients.

Results to Date:

There are approximately 55 smokers' clinics in the United Kingdom. Although services were started by doctors, most (62 percent) were being run by health education officers. Others involved included doctors, health visitors, and clinical psychologists. Most clinics offered group support over several weeks with some information about health risks. Few have incorporated nicotine gum as a withdrawal aid, partly because of its status as a prescription-only medicine. Publicity and recruitment procedures vary considerably as does throughput. The busiest clinics see from 200 to 500 new clients/year. Even with an average cessation rate of 25 percent, this means that if each district in England and Wales had such a service, they could help from 10,000 to 15,000 smokers to quit each year. Such a service could be run with resources already available and the ideal infrastructure for developing support services already exists with the emergence of multidisciplinary teams in primary health care. The success of health education programs has meant a greater demand for support from those who cannot stop unaided. The two major approaches must be to persuade smokers that they ought to stop and to provide the support to help them do so. Recommendations made for the future suggest that (1) each district health authority (DHA) should have a smoking prevention policy; (2) the policy should include a cessation component; (3) the policy should be implemented; (4) each DHA should form a health promotion team to develop policy and monitor its implementation; (5) each policy should state priorities and outline a realistic timetable for implementation; and (6) a national center should be established to advise health authorities and national bodies on cessation.

Project Dates:

November 1980–1983.

Financial Support:

Health Education Council, England and Wales.

Reference:

Raw, M.; Heller, J. "Helping People to Stop Smoking." London, The Health Education Council, 1984, 134 pp.

0554. ST. GEORGE'S HOSPITAL, MEDICAL SCHOOL, Cranmer Terrace, London SW17 0RE, England.

Project Title:

Effectiveness of Nicotine Chewing Gum in Relation to Duration of Use.

Principal Investigator:

Raw, M.

Objective:

To determine if duration of use of nicotine gum is related to efficacy in promoting abstinence from smoking, as suggested in the literature.

Methods or Approach:

Groups of approximately 10 to 20 smokers are assigned in a balanced order to one of two treatment conditions: (1) support plus nicotine gum for as long as required; or (2) support plus 1 month of nicotine gum. Both groups will receive initial orientation and weekly sessions over a 1-month period. Followup sessions will be held in the second and third months. Long-term followup will be at 6 and 12 months.

Results to Date:

Results are not yet available.

Project Dates:

November 1983–October 1985.

Financial Support:

AB Leo Pharmaceuticals, Helsingborg, Sweden.

0555. ST. GEORGE'S HOSPITAL, MEDICAL SCHOOL, Cranmer Terrace, London SW17 0RE, England.

Project Title:

Nutrition, Psychosocial Stress and Smoking in Pregnancy and Their Effects on Birth Size and Length of Gestation.

Principal Investigators:

Brooke, O.G.; Anderson, H.R.

Objective:

To examine the relationship between dietary intake and biochemical indices of nutrition in a representative sample of smoking and nonsmoking women; study relationship between psychosocial stress, smoking, birth weight, and length of gestation in a whole population of pregnant women.

Methods or Approach:

Psychosocial stress is investigated by questionnaire at four pregnancy intervals, in addition to detailed information about smoking habits and ingestion of potentially toxic substances such as alcohol. In the nutritional study subsample, 200 women will be investigated by weighed food intake over two 1-week periods, together with detailed biochemical and anthropometric assessment. All data collected in the population study will also be collected in the nutrition subsample.

Results to Date:

Fieldwork has been completed, but results are not yet available.

Project Dates:

1980–1986.

Financial Support:

Tobacco Companies Consortium.

0556. ST. THOMAS'S HOSPITAL, London, SW1, England.

Project Title:

Cyanide Metabolism in Leber's Hereditary Atrophy, W. Indian Amblyopia, and "Tobacco-Alcohol Amblyopia."

Principal Investigators:

Pool, J.; Kind, P.R.N.

Objective:

To (1) confirm abnormality of cyanide metabolism in Leber's disease; (2) demonstrate reduction in rhodanese (thiosulfate:cyanide sulfurtransferase) in amblyopia patients; and (3) confirm mitochondrial inheritance.

Methods or Approach:

Rhodanese activity was measured in rectal mucosa of amblyopia patients and their first-degree relatives.

Results to Date:

Results tend to confirm earlier observations of reduced rhodanese activity.

Project Dates:

1983–continuing.

Financial Support:
D.M.S.S., United Kingdom.

0557. THE MAUDSLEY HOSPITAL, SMOKERS CLINIC, Denmark Hill, London SE5 8AZ, England.

Project Title:
Long-Term Community Programme for Intervention Against Smoking.

Principal Investigators:
Russell, M.A.H.; Hajek, P.; Belcher, M.

Objective:
To develop and evaluate ways in which a smokers clinic could function as a center for instigating and coordinating multiple approaches to reduce prevalence of smoking within the whole local community; develop and evaluate more effective methods to help people give up smoking.

Methods or Approach:
The Smokers Clinic provides intensive treatment for about 300 dependent smokers/year using mainly group support plus nicotine chewing gum; however, refinements and new approaches are also tested. The major task is development of a wider role as a center for mobilizing intervention by other health professionals in the local district. In the first phase, focus was on family physicians. More than 100 have been recruited, including those in a control district. Effect of their intervention has been assessed by a longitudinal study of over 4,000 of their patients who smoke cigarettes. The cumulative effect of continued routine intervention is being assessed by a series of prevalence surveys every 6 months, each survey involving about 10,000 patients.

Results to Date:
Efficacy of nicotine gum compared with placebo gum and of group-oriented compared with therapist-oriented format of group treatment was demonstrated. A pilot acceptability study of a nasal nicotine solution (liquid snuff) has also been completed. Controlled longitudinal studies have demonstrated efficacy of brief intervention by family physicians, which was more effective when nicotine gum was offered in addition to advice and leaflets. Preliminary results of the 6-month prevalence surveys indicate a decline in prevalence of smoking among patients of physicians who practice intervention, but no change in patients of physicians in the control district. However, for definitive evaluation of the cumulative effect, results of surveys scheduled for 3 and 3.5 years after start of intervention will be assessed.

Future Plans:
Additional brief interventions by other health professionals (health visitors and pharmacists) will be initiated and combined effects will be evaluated.

Project Dates:
April 1981–April 1988.

Financial Support:
U.K., Department of Health and Social Security (7415).

0558. UNIVERSITY HOSPITAL OF SOUTH MANCHESTER, Department of Epidemiology and Social Research, Kinnaird Road, Withington, Manchester M20 9QL, England.

Project Title:
Changes in the Smoking Behaviour, Knowledge and Opinion of Medical Students 1972-1981.

Principal Investigator:
Elkind, A.K.

Objective:
To repeat a 1972 survey of medical students at Manchester University to determine changes in smoking behavior, knowledge, and opinion from 1972 to 1981; examine students' view of the doctor's role in relation to smoking.

Methods or Approach:
Students were sent a postal questionnaire; 1,112 replied (96 percent response). Data were compared with results from a similar survey in 1972.

Results to Date:
Cigarette smoking declined substantially between 1972 and 1981, similar to trends in the general population, indicating that medical education has contributed little to the change. In 1981, 17 percent of medical students were cigarette smokers compared with 29 percent in 1972. The decline was more marked in male students than in female students, and was already evident before students began their medical studies. Modest changes had also occurred in knowledge and opinions about smoking. The smoking behavior of patients was recognized as an important concern of the doctor. However, smokers were equivocal about the implications of private behavior on the doctor's professional role.

Project Dates:
1981–1982.

Financial Support:
U.K. Department of Health and Social Security.

References:
(1) Elkind, A.K. "Changes in the Smoking Behaviour, Knowledge and Opinion of Medical Students 1972-1981." *Social Science and Medicine* 16:2137-2143, 1982. (2) Elkind, A.K. "Smoking: How Medical Students See the Doctor's Role." *Public Health* 97:38-45, 1983. (3) Elkind, A.K. "Anonymity or Identification? Offering the Choice in a Survey of Smoking. *Journal of the Institute of Health Education* 22:27-30, 1984.

0559. UNIVERSITY HOSPITAL OF SOUTH MANCHESTER, Department of Epidemiology and Social Research, Kinnaird Road, Withington, Manchester M20 9QL, England.

Project Title:
Changes in the Smoking Behavior, Knowledge and Opinion of Nurses and Student Teachers During the First Year of Professional Training.

Principal Investigator:
Elkind, A.K.

Objective:
To (1) determine whether smoking behavior of female nurses and teachers can be explained by the smoking behavior of women in general or by aspects of training; (2) examine patterns of behavior at entry to training and factors involved in changes during the first year; (3) examine knowledge and opinion of smoking and view of the professional role in smoking education that future nurses and teachers bring with them to training; and (4) determine changes that occur during the first year.

Methods or Approach:
Questionnaires and interviews were utilized in the longitudinal study of 115 students; three groups of nurses (general students, pediatric students, and pupils) and one group of teachers. Students began training in the fall of 1980 and were followed up for 1 year.

Results to Date:
At entry to training, learner nurses were twice as likely to be smokers as student teachers (33 percent vs. 16 percent, respectively). There were also marked differences between the

three groups of nurses that reflected variations found among qualified nurses and teachers. Results unexpectedly indicated that, in relation to the wider context of women's behavior, smoking may still be perceived in terms of a negative cultural stereotype. In a later phase of the study that examined images of female smokers and nonsmokers, the nonsmoker's image of smokers was based on the stereotypic view (unladylike), whereas smokers saw other female smokers as "liberated." Nonsmokers saw other female nonsmokers as "feminine." Smokers had no clear view of female nonsmokers.

Project Dates:
1980–1985.

Financial Support:
U.K. Department of Health and Social Security.

Reference:
Elkind, A.K. "The Social Definition of Women's Smoking Behaviour." *Social Science and Medicine* (In press).

0560. UNIVERSITY OF BRISTOL, Department of Epidemiology and Community Medicine, Canynge Hall, Whiteladies Road, Bristol BS8 2PR, England.

Project Title:
Medical Research Council National Survey of Health and Development.

Principal Investigators:
Colley, J.R.T.; Wadsworth, M.E.J.

Objective:
To monitor the behavior and health of a sample of 5,000 persons followed since birth in 1946; assess how smoking and factors associated with smoking are related to morbidity.

Methods or Approach:
The cohort study has followed up one in three of all legitimate single births in Britain from March 3 to March 9, 1946. Contact has been made at least every 2 years, and three medical examinations have been carried out. Complete records have been kept of hospital admissions and outpatient visits, and consultations with general practitioners have been recorded. Data on cough have been collected by a standardized questionnaire. Smoking habits are known through self-reports made at ages 20 years, 25 years, 31 years, and 36 years, and at the latter age measures have been made of respiratory peak flow and of blood pressure. Personality tests were given at age 16 to 2,753 people.

Results to Date:
The results of personality tests indicated that (1) neurotics were more likely to smoke than non-neurotics; (2) extroverts were more likely to smoke than introverts, especially males; and (3) deep inhalers were the most neurotic group. The test predicts that stable, extroverted males are the group most likely to give up smoking by age 25. A survey of respiratory symptoms and smoking habits of the subjects at 20 years of age and again at 25 years of age showed that (1) cough related to current smoking habits and lower respiratory tract illness in childhood increased over 5 years; (2) at age 25 the cough was significantly associated with the father's occupation; (3) the influence of air pollution on cough is not clear; and (4) the cough declined in nonsmokers and ex-smokers.

Future Plans:
This project is on-going. Information about smoking behavior is now being collected at each contact. Data collection at 36 years is being analyzed to examine associations between smoking behavior and lifetime histories of respiratory illness. It will also be possible to update the earlier work from this study on smoking habits and personality factors.

Project Dates:
March 1946–continuing.

Financial Support:
University of Bristol; MRC, United Kingdom.

0561. UNIVERSITY OF CAMBRIDGE, ADDENBROOKE'S HOSPITAL, Department of Medicine, Hills Road, Cambridge CB2 2QQ, England.

Project Title:
Individual Differences in Smoking Motivation.

Principal Investigator:
Surawy, C.J.

Objective:
To validate a typology based on the assumption that smokers use nicotine to produce changes in levels of arousal, such changes being dependent on the smoker's "resting" level of arousal and personality.

Methods or Approach:
Three experiments tested the hypothesis that smokers may be categorized according to conditions under which they prefer to smoke. Subjects were selected according to questionnaire responses that separated smokers into two groups: (1) sedative smokers, who report smoking predominantly under "high arousal" conditions such as anxiety, ostensibly to decrease arousal; and (2) stimulant smokers, who report smoking predominantly under "low arousal" conditions, probably to increase arousal. Personality was measured with the Eysenck Personality Questionnaire. In the first experiment, smokers were given an opportunity to smoke under conditions of relaxation (pleasant, low arousal) and noise (unpleasant, high arousal) and behavior was studied. Comparable conditions in which smoking was not allowed were used for controls. Measurements were made of heart rate, heart rate variability, mouth level nicotine intake, puff rate, number of cigarettes smoked, and self-reported stress and arousal. In the second experiment, an attempt was made to isolate variables (measured by self-reported stress and arousal and smoking context) that are most salient as triggers for smoking under nonlaboratory conditions. Subjects were required to self-monitor smoking behavior for 1 day, recording desire for and enjoyment of each cigarette smoked. Butt analysis of all cigarettes smoked was used as an indirect measure of nicotine levels. On the basis of findings from the first two experiments, responses of sedative and stimulant smokers to social cues was investigated, using a within subjects design. Puff rate, number of cigarettes smoked, and latency to light up were measured in two conditions (with and without smoking cues).

Results to Date:
Data indicate that although differences in patterns of behavior were observed, differences were not in accordance with predictions. Sedative smokers were more neurotic, smoked more, and expressed a greater desire for smoking under conditions perceived as relatively stressful, irrespective of concomitant level of arousal. Mouth level of nicotine, however, varied under conditions of high stress according to perceived arousal. Nicotine exposure was higher under conditions of high stress and high arousal than under high stress and low arousal, suggesting that in the former, the sedating effect on arousal of a larger dose of nicotine was being sought, while in the latter, an alerting effect was desired. It is suggested that sedative smokers may use the arousal-altering properties of nicotine to increase well-being (reduce stress) under a variety of conditions. Smoking behavior of stimulant smokers was unaffected by perceived level of stress or arousal, but was influenced greatly by presence of smoking cues. The higher levels of

extraversion in stimulant smokers may predispose them to continually "scan" the environment for potential sources of stimulation, resulting in greater susceptibility to environmental smoking cues. Results suggest that considering smoking behavior exclusively in terms of the unitary concept of arousal masks important differences between smokers, and does little to develop the present state of knowledge concerning relationships between perceived reasons for smoking and actual behavior.

Project Dates:
October 1981–March 1985.

Financial Support:
Imperial Tobacco Company Ltd.

Reference:
Surawy, C.J.; Stepney, R.; Cox, T. "Does Watching Others Smoke Increase Smoking?" *British Journal of Addiction* (In press).

0562. UNIVERSITY OF EXETER, WASHINGTON SINGER LABORATORIES, Perry Road, Exeter, Devon EX4 4QG, England.

Project Title:
Strategic Research in Health Education.

Principal Investigator:
Eiser, J.R.

Objective:
To (1) provide a broad theoretical and methodological research base for health education practice and policy in a number of priority areas, including cigarette smoking; (2) identify areas of insufficient health knowledge where improved communications may be effective; and (3) understand how psychological factors such as attitudes, cognitive and social development, and group membership may influence people's interpretation of health information and the decisions that are made regarding health and lifestyle.

Methods or Approach:
A wide variety of methods have been used, ranging from individual interviews (school students, parents, pregnant women, children with chronic illnesses such as diabetes, asthma, coronary disease) to postal or group-administered questionnaires. All methods are direct toward understanding the structure of individual beliefs and decisions about health and illness.

Results to Date:
Results suggest that smoking is related to a broad spectrum of other health values and behaviors. Although people rely on intuitive causal theories relating smoking to ill health (not exclusively cancer), they tend to have a rather poor appreciation of statistical ideas of risk and of the extra risk involved with smoking compared with other habits. With adults, data validate the hypothesis of the coronary-prone behavior syndrome in a British population. When aspects of behavior people believe contribute to coronary-prone behavior are considered, smoking is included. Studies concerned with children's acquisition of concepts of health, illness, and bodily processes have also related children's understanding of smoking to more general cognitive developmental processes.

Future Plans:
Analyses will be made on data relevant to applicability of the Fishbein-Ajzen model of attitudes and behavior relationships to smoking and other health behaviors.

Project Dates:
October 1980–October 1985.

Financial Support:
Health Education Council, London.

0563. UNIVERSITY OF EXETER, WASHINGTON SINGER LABORATORIES, Perry Road, Exeter, Devon EX4 4QG, England.

Project Title:
Smoking Education for Teenagers - Video Films.

Principal Investigator:
Eiser, J.R.

Objective:
To (1) assess potential usefulness of teaching materials to deter smoking by adolescents, based on the concept of resistance to social pressures; (2) provide data on prevalence of smoking behavior and attitudes among adolescents; and (3) develop teaching materials suitable for dissemination in British schools.

Methods or Approach:
A major questionnaire study was conducted of smoking prevalence and attitudes among approximately 10,500 11- to 16-year-olds in the County of Avon, England. Self-reports have been checked against salivary cotinine levels in a subsample. The video films have been designed to increase adolescents' awareness of different forms of social pressure (peers, adults, commercial advertising) and to indicate how such influences can be resisted amd how individuals can take responsibility for their own and others' health.

Results to Date:
Results indicate that 69 percent of the total sample had at least tried smoking, and of these, 61 percent of the boys and 45 percent of the girls had done so by age 11. Percentages of regular smokers by age group was 9 percent at age ll, 11 percent at age 12, 17 percent at age 13, 28 percent at age 14, 34 percent at age 15, and 38 percent at age 16. Pupils greatly overestimated the true percentage of smokers (11-year-olds estimated that 25 percent of their age group smoked). Pupils who smoked reported drinking more and receiving more spending money and did not do as well in school as nonsmokers. The strongest predictors of smoking were the beliefs that smoking is enjoyable and that parents and friends would not mind if students smoked.

Future Plans:
Reactions by teachers and other students will be assessed, and further analyses of study data will be conducted, particularly the interrelationships between friendship patterns and shared health habits (smoking, alcohol).

Project Dates:
October 1980–October 1985.

Financial Support:
Health Education Council, London.

0564. UNIVERSITY OF LEEDS, Department of Medical Physics, The General Infirmary, Leeds, West Yorkshire LS1 3EX, England.

Project Title:
Tests of Causal, Constitutional, and Mixed Hypotheses of Associations Between Smoking and Disease in Man.

Principal Investigator:
Burch, P.R.J.

Objective:
To assess the risks of smoking in man.

Methods or Approach:
The project includes analysis of cohort and period trends in mortality in relation to corresponding trends in cigarette consumption and of the dependence on age of sex- and age-specific disease onset and death rates.

Results to Date:
Recent secular trends in sex- and age-specific mortality from

ischemic heart disease, both in the United Kingdom and in the United States, appear to be independent of changes in cigarette consumption. Secular trends in mortality from esophageal cancer in the United Kingdom are independent of secular changes in cigarette consumption, but well correlated with secular changes in alcohol consumption. Sex and age patterns of mortality are also consistent with the hypothesis that alcohol acts as an indirect causal agent. The proximal causal agent is likely to be a precipitator, such as a microorganism. Genetic predisposition is also implicated.

Project Dates:
1972–continuing.

Financial Support:
University of Leeds.

0565. UNIVERSITY OF LONDON, SCHOOL OF HYGIENE AND TROPICAL MEDICINE, TUC Centenary Institute of Occupational Health, Keppel Street, London WC1E 7HT, England. MEDICAL RESEARCH COUNCIL, Pneumoconiosis Research Unit, Penarth, Cardiff, Wales.

Project Title:
Cancer of the Lung Among Asbestos Factory Workers.

Principal Investigators:
Berry, G.; Newhouse, M.L.

Objective:
To assess the interaction of smoking and asbestos on mortality from lung cancer.

Methods or Approach:
Smoking habits of male and female asbestos workers were ascertained in 1971 and mortality followed to 1980. Smoking habits of certain proportions of the cohort were also obtained at time of death.

Results to Date:
Data from the 1970-1980 prospective study have now been analyzed. After allowing for the effect of smoking on lung cancer, the relative risk due to asbestos was highest for those who had never smoked, lowest for current smokers, and intermediate for ex-smokers. The trend was statistically significant. There was no significant association between smoking and deaths from mesothelioma. Followup of smoking habits at time of death showed changes in smoking habit in some subjects since the original survey, which may have influenced final results.

Project Dates:
1970–completed.

Financial Support:
MRC, United Kingdom.

0566. UNIVERSITY OF LONDON, INSTITUTE OF PSYCHIATRY, Denmark Hill, London SE5 8AF, England.

Project Title:
Cross-Cultural Relationships Between Smoking, Personality, and Health.

Principal Investigators:
Eysenck, H.J.; Eysenck, S.B.G.; Barrett, P.

Objective:
To conduct a cross-sectional project to test the theory that personality factors are related to both smoking and cancer.

Methods or Approach:
A previous study showed highly significant correlations between personality and various types of cancer, while failing to find any correlation between smoking and cancer; therefore, 25 diverse national or cultural groups are being tested with the Eysenck Personality Questionnaire (minimum 500 male and 500 female subjects). Factor analyses of intercorrelations between items are carried out, and resulting factors compared among all 25 national groups by means of indices of factor comparison. Resulting factors are then correlated with such items as tobacco consumption, incidence of lung cancer, other types of illness, and approximately 130 demographic measures thought to be relevant to the issue.

Results to Date:
Findings to date show that personality factors appearing in the 25 national groups are very similar, indices of factor comparison averaging above 0.98. It is thus concluded that the rest of the test will be meaningful, and data are being analyzed.

Project Dates:
September 1983–September 1986.

Financial Support:
CRT.

0567. UNIVERSITY OF LONDON, INSTITUTE OF PSYCHIATRY, Denmark Hill, London SE5 8AF, England.

Project Title:
Personality and the Psychological Effects of Smoking.

Principal Investigators:
Eysenck, H.J.; O'Conner, K.

Objective:
To investigate the psychological effects of smoking; particularly with respect to the CNV, as influenced by personality factors.

Methods or Approach:
Subjects are administered the Eysenck Personality Questionnaire (with particular reference to status as extroverts or introverts), and tested under a variety of conditions to elicit psychophysiological responses, particularly the CNV. An effort is made to relate personality to type of responses. Sham-smoking conditions are compared with real smoking conditions, and certain hypotheses (developed by Eysenck) are tested.

Results to Date:
Results indicated a powerful interaction between personality and effects of smoking. Quite frequently it was found that the effects on extroverts are the opposite of effects on introverts.

Project Dates:
January 1979–December 1984.

Financial Support:
Reynolds Tobacco Research.

0568. UNIVERSITY OF NOTTINGHAM, UNIVERSITY HOSPITAL AND MEDICAL SCHOOL, Department of Community Health, Nottingham, England.

Project Title:
Evaluation of the Health Education Council My Body Project.

Principal Investigator:
Gillies, P.A.

Objective:
To evaluate the long-term effects of a primary school health education project with an antismoking component on pupils' smoking behavior and knowledge of and attitudes toward smoking.

Methods or Approach:
Children aged 9 to 11 from three primary schools using the "My Body" project were matched with students from three control schools for social class, school size, school type, and

geographical position. Both groups have been followed since 1980; attrition rate was 14 percent in experimental schools and 17 percent in control schools. Information on smoking behavior and knowledge was recorded from self-administered questionnaires before the project began and at yearly intervals thereafter.

Results to Date:
No differences between intervention and control groups were observed at pretesting. Of those who had never smoked before the project began, twice as many control students as program students had experimented with smoking 1 and 2 years later, suggesting that the project had a beneficial effect on preventing smoking onset.

Project Dates:
January 1980–June 1985.

Financial Support:
Health Education Council, London.

0569. UNIVERSITY OF NOTTINGHAM, UNIVERSITY HOSPITAL AND MEDICAL SCHOOL, Department of Community Health, Clifton Boulevard, Nottingham NG7 2UH, England.

Project Title:
Quantification of Passive Exposure to Smoking in Children.

Principal Investigators:
Gillies, P.A.; Pearson, J.C.G.

Objective:
To quantify, by noninvasive means, immediate physical changes in young children that result from passive exposure to cigarette smoke in the home environment.

Methods or Approach:
Samples of expired air were collected from children (aged 10 to 11 years) in 1L bags. Children were asked to breathe out normally and hold for 10 seconds before blowing into the bag. Samples were analyzed immediately, using a carbon monoxide (CO) monitor with an electrochemical cell (method reliability, $r = 0.98$). CO levels minus ambient CO were recorded. Details of smoking by children, parental smoking in the home, and exposure to other forms of CO pollution were collected by standard questionnaire.

Results to Date:
A statistically significant relationship was found between increasing CO levels in children and the number of parents who smoked. Children from homes in which both parents smoked had the highest mean levels of CO in expired air. The trend of increasing CO levels with parents who smoked was still observed when smoking by children was taken into account, but was not statistically significant.

Future Plans:
The effect of passive smoking on expired CO levels in very young (preschool) children will be investigated in a prospective study to relate recorded levels with episodes of respiratory illness.

Project Dates:
June 1982–1985.

Financial Support:
Health Education Council, London.

0570. UNIVERSITY OF OXFORD, RADCLIFFE INFIRMARY, Department of Community Medicine and General Practice, Oxford OX2 6HE, England.

Project Title:
Randomised Control Trial of the Effectiveness of Antismoking Intervention by Nurses in General Practice.

Principal Investigators:
Fowler, G.; Sanders, D.; Marziller, J.

Objective:
To demonstrate effectiveness of nurses giving antismoking advice in general practice.

Methods or Approach:
Patients (all smokers ≥ 16 years of age), attending the practice during the recruitment period, are randomized by day of attendance. On control days, patients receive no intervention. On intervention days, smokers are invited to see a nurse for a brief health check. As part of the checkup, the nurse gives brief antismoking advice and provides a Give Up Smoking leaflet. In the second intervention group, the advice and leaflet are supplemented with a demonstration of the level of carbon monoxide in patient's expired breath. Patients will be followed by postal questionnaire at 3 months and 1 year after initial consultation. Self-reported smoking cessation will be validated by measurement of cotinine in urine samples obtained during unannounced home visits.

Results to Date:
Project is in a preliminary phase.

Project Dates:
September 1984–June 1987.

Financial Support:
British Heart Foundation; British Education Council.

0571. UNIVERSITY OF OXFORD, RADCLIFFE INFIRMARY, Department of Community Medicine and General Practice, Oxford OX2 6HE, England.

Project Title:
Placebo Controlled Trial of Nicotine Chewing Gum in General Practice.

Principal Investigators:
Jamrozik, K.; Fowler, G.; Vessey, M., et al.

Objective:
To assess effectiveness of nicotine chewing gum as an aid to smoking cessation in patients in general practice.

Methods or Approach:
Patients were participants of an "advice" program who had tried to quit but had failed. Patients were offered a "new special chewing gum" (nicotine gum or placebo gum identical in appearance and packaging) in a double-blind, randomized controlled trial. Subjects were asked to see doctors for followup at 2, 4, and 12 weeks following initial visit. After 6 months, participants were paid an unannounced home visit and questioned about smoking habits. Self-reported cessation was validated by analysis of expired carbon monoxide.

Results to Date:
Of eligible patients, 200 (47 percent) accepted offer of gum; 101 received nicotine gum and 99 received placebo gum. At 6-month followup, 25 claimed to have stopped smoking, but 7 exhaled levels of CO indicative of continued smoking. Of the 18 in whom cessation was validated, 10 had received nicotine gum and 8 placebo gum, a difference that is not significant.

Project Dates:
March 1982–March 1983.

Financial Support:
Oxford District Research Committee; Nuffield Dominions Trust and Lundbeck Ltd.

0572. UNIVERSITY OF OXFORD, RADCLIFFE INFIRMARY, Department of Community Medicine and General Practice, Oxford OX2 6HE, England.

Project Title:
Controlled Trial of Three Different Antismoking Interventions in General Practice.

Principal Investigators:
Jamrozik, K.; Vessey, M.; Fowler, G., et al.

Objective:
To (1) demonstrate whether verbal and written antismoking advice from general practitioners, given in ordinary consultations, is effective in helping patients stop smoking; (2) determine whether demonstration of exhaled carbon monoxide (CO) is an effective antismoking intervention; and (3) determine whether the offer of further help from a health visitor (public health nurse) is effective.

Methods or Approach:
In the six general practices that participated, just over 2,000 patients (over 16 years of age) who smoked were recruited, randomized for the controlled trial according to day of attendance. Treatments included (1) verbal advice plus leaflet on giving up smoking; (2) the same, with addition of a demonstration of exhaled CO; and (3) the same as (1), with addition of offer of health visitor at followup. All participants received a followup questionnaire at the end of 1 year. Validation of self-reported cessation was by measurement of cotinine in urine samples obtained during unannounced home visit.

Results to Date:
A 72 percent followup rate was achieved; however, results are based on the assumption that nonresponders continued smoking. Proportion who reported smoking cessation a 1-year followup was 15 percent of group 1, 17.2 percent of group 2, and 13.2 percent of group 3. Average for all participants was 15.2 percent; for controls, 10.6 percent were able to quit. Comparison of the four groups, $\chi^2 = 8.5$; 3 df; $p<0.05$. Comparison of all intervention groups with control group, $\chi^2 = 5.8$; 1 df; $p<0.02$. Values have been adjusted for effect of social class.

Future Plans:
A similar study will be conducted to determine effectiveness of nurses rather than doctors.

Project Dates:
October 1980–March 1983.

Financial Support:
Health Education Council, England.

England.

0573. UNIVERSITY OF OXFORD, Department of Paediatrics, John Radcliffe Hospital, Headington, Oxford OX3 9DU, England.

Project Title:
Effect of Maternal Smoking During Pregnancy on Fetal Growth and Child Development.

Principal Investigators:
Ounsted, M.; Scott, A.

Objective:
To study effects of maternal smoking on fetal growth rate and child development.

Methods or Approach:
The project is part of a larger study linking pregnancy and delivery factors with pre- and postnatal growth and development. Large cohorts of small-for-date (SFD), average-for-date (AFD), and large-for-date (LFD) infants have been ascertained at birth. In a separate study, hypertensive pregnant women have or have not been randomly allocated to specific therapy. All infants are examined regularly from birth to 7 years of age. On each occasion, a history is taken and assessments are made of growth and development.

Results to Date:
Estimates of relative risk showed that smoking during pregnancy tripled chances of having a SFD baby. The comparable attributable risk value (39.7 percent) indicated that if smoking could be completely eliminated, the number of SFD babies in the study population would be reduced by nearly 40 percent. Nonsmoking doubled the risk of having a LFD baby. The estimated contribution to the LFD population as a whole was 43.7 percent. After adjustment for confounding between variables, maternal smoking during pregnancy did not make a significant contribution to weight, height, or head circumference of children at 7 years of age. It did make a small contribution (3.4 percent, $p<0.05$) to intellectual ability of AFD children at age 7 years, but had no effect on SFD or LFD children.

Project Dates:
1964–1985.

Financial Support:
MRC, United Kingdom.

0574. UNIVERSITY OF READING, Department of Psychology, Building 3, Earley Gate, Whiteknights, Reading, Berkshire RG6 2AL, England.

Project Title:
The Effects of Cigarette Smoking on Human Information Processing and the Role of Nicotine in These Effects.

Principal Investigators:
Warburton, D.M.; Wesnes, K.

Objective:
To (1) determine effects of cigarette smoking on human information processing; (2) determine role played by nicotine in improvements in information processing produced by smoking; and (3) determine neurochemical and physiological processes by which nicotine improves human information processing.

Methods or Approach:
Volunteer smokers perform computerized tests of information processing ability before, during, and after smoking. Nicotine tablets are also presented to determine role of nicotine. Scopolamine is used to block nicotine effects and thus determine cholinergic involvement in effects of smoking. EEG and arrayed visual evoked potentials are also recorded to determine the electrophysiological basis of behavioral effects.

Results to Date:
Findings indicate that (1) smoking improves human information processing; (2) higher nicotine cigarettes produce greater improvements than low-nicotine cigarettes; (3) nicotine tablets produce similar effects; (4) nicotine can reverse the detrimental

effects of scopolamine on performance; and (5) smoking effects are accompanied by increases in EEG arousal and decreases in the latency of the late positive component of the evoked potential.
Future Plans:
An attempt will be made to categorize those smokers in whom information processing is consistently improved; investigate the role of nicotine in improvements; and determine more precisely the neurochemical and electrophysiological bases of the effects.
Project Dates:
1977–continuing.
Financial Support:
MRC, United Kingdom.

England.

0575. UNIVERSITY OF SHEFFIELD, Department of Anatomy and Cell Biology, Sheffield S10 2TN, England.

Project Title:
Cell Replacement Rates in Human Bronchial Epithelium.

Principal Investigators:
Rogers, A.W.; Watanabe, M.
Objective:
To determine cell replacement rate in human bronchial epithelium; relate findings to histological structure of the epithelium (normal, mucous hyperplasia, or squamous metaplasia) measured morphometrically.
Methods or Approach:
Data on epithelial structure and cell replacement rates are being studied in nonsmokers, current smokers, and ex-smokers, and correlated with epidemiological findings on the probability of developing bronchial carcinoma. Biopsy specimens of bronchial mucosa are cultured in the presence of tritiated thymidine and autoradiographed. Cell replacement rate is calculated and plotted against the histological state of the epithelium, expressed as a numerical index, which is derived from previously described morphometric measurements.
Results to Date:
Project is in a preliminary phase.
Project Dates:
October 1984–October 1986.
Financial Support:
University of Sheffield.

0576. UNIVERSITY OF SOUTHAMPTON, Department of Psychology, Southampton SO9 5NH, England.

Project Title:
Evaluation of Self-Help Community Stop-Smoking Groups in Wessex Region (Operation Smokestop).

Principal Investigators:
Batten, L.; Taylor, D.H.
Objective:
To set up, maintain, and evaluate a program of self-help stop-smoking groups throughout Hampshire, Wiltshire, Dorset, and the Isle of Wight (Wessex region, population approximately 2,750,000).
Methods or Approach:
Two hundred people attended training workshops designed to introduce participants to the skills required for effective group facilitation. Subsequently, networks of group leaders were encouraged for support and further training. Promotional work with television, radio, and the press was conducted, with a central telephone inquiry service for referral of smokers to groups. Data were collected on all participants.
Results to Date:
Fifty group leaders have been active in 30 urban locations. During evaluation, 715 smokers attended groups, and cessation at 1 year ranged between 15 and 30 percent of all attendees. Group leaders are mostly health professionals, which has led to greater involvement by health authorities in planning intervention strategies. The self-help network is being coordinated by health authorities in Wessex through Health Education Units. Other health authorities are now following the model created and are beginning to implement integrated community-based smoking cessation programs.
Project Dates:
January 1982–April 1985.
Financial Support:
Cancer Research Campaign, United Kingdom.

0577. UNIVERSITY OF SOUTHAMPTON, SOUTHAMPTON GENERAL HOSPITAL, Department of Chemical Pathology and Human Metabolism, and Faculty of Medicine, Professorial Medical Unit, Southampton S09 4XY, England.

Project Title:
Effect of Smoking, Alcohol, and Other Factors on the Selenium Status of a Healthy Population.

Principal Investigators:
Lloyd, B.; Lloyd, R.S.; Clayton, B.E.
Objective:
To establish reference ranges for blood selenium and glutathione peroxidase; determine effect of diet, smoking, alcohol intake, and oral contraceptive use.
Methods or Approach:
Blood samples were taken from 391 apparently healthy subjects (228 men and 163 women) residing in the south of England. Age range was from 18 to 85 years. Samples were assayed for selenium and glutathione peroxidase activity, and for routine hematological parameters. Alcohol consumption and smoking habits were recorded, and women were asked about use of oral contraceptives.
Results to Date:
Reference ranges were established for glutathione peroxidase activities and for concentrations of selenium in whole blood, plasma, and erythrocytes. Data showed that age, smoking, alcohol consumption, and use of oral contraceptives had a significant effect. The most important factors appeared to be a combination of alcohol use and smoking in men over 30 years of age.
Project Dates:
January 1982–March 1983.
Financial Support:
Southampton University.

0578. UNIVERSITY OF SOUTHAMPTON, Department of Chemical Pathology and Human Metabolism, and Faculty of Medicine, Professorial Medical Unit, Southampton S09 4XY, England.

Project Title:
Selenium and Vitamin E in Relation to Risk Factors for Coronary Heart Disease.

Principal Investigators:
Ellis, N.; Lloyd, B.; Lloyd, R.S., et al.
Objective:
To study the relationship between blood lipids, trace elements, and cigarette smoking in apparently healthy men; determine whether any other factors may be important.
Methods or Approach:
Fasting blood samples were taken from 116 apparently healthy men aged 30 to 50 years and assayed for selenium, glutathione peroxidase activity, vitamin E, cadmium, lead, glucose, lipids, and albumin. Blood pressure was measured and details of height, weight, smoking habits, and alcohol consumption were recorded.
Results to Date:
Cigarette smokers had significantly lower concentrations of blood and serum selenium than nonsmokers, and an increase in whole blood cadmium concentrations. Multivariate analysis of data showed results to be independent of alcohol consumption. There was no correlation between blood selenium concentrations or glutathione peroxidase activities and risk factors for cardiovascular disease. There was a strong association between vitamin E and serum lipid concentrations; however, neither alcohol consumption nor smoking had any effect on concentrations of vitamin E in serum.
Project Dates:
October 1982–November 1983.
Financial Support:
Wessex Regional Health Authority.

0579. UNIVERSITY OF SUSSEX, DEVELOPMENTAL PSYCHOLOGY GROUP, Falmer, Brighton, East Sussex BN1 9QN, England.

Project Title:
Effects of Cigarette Smoking in Different Types of Smokers.

Principal Investigators:
Williams, D.G.; Tata, P.R.; Miskella, J.
Objective:
To compare reactions to the first cigarette of the day by smokers who generally prefer to smoke in high arousal situations and smokers who prefer low arousal situations.
Methods or Approach:
In a moderately relaxed setting, smokers were asked to smoke their first cigarette of the day in the following manner: two 2-second puffs/minute until a line drawn at 5 mm from the filter overwrap was reached.
Results to Date:
In both male and female smokers, pulse rates were elevated after smoking and performance in a letter cancellation task was faster. However, high arousal situation smokers and low arousal situation smokers of either sex did not differ in the size of the changes. Published results discuss specific and general reservations about partitioning smokers into "types."
Project Dates:
February 1980–completed.
Financial Support:
University of Sussex, England.
Reference:
Williams, D.G.; Tata, P.R., Miskella, J. "Different 'Types' of Cigarette Smokers Received Similar Effects After Smoking." *Addictive Behaviors* 9:207-210, 1984.

Scotland.

0580. DUNDEE UNIVERSITY, NINEWELLS HOSPITAL AND MEDICAL SCHOOL, Department of Therapeutics, Dundee DD1 9SY, Scotland.

Project Title:
The Effects of Smoking on Meal-Stimulated Gastric Secretion, Gastric Emptying and the Disposition of Histamine H_2-Receptor Antagonists.

Principal Investigators:
Boyd, E.J.S.; Jonstone, D.A.; Wilson, J.A., et al.
Objective:
To study effects of smoking on meal-stimulated gastric secretion and rate of gastric emptying, with and without pretreatment with histamine H_2-blockers; investigate effects of smoking on disposition of H_2-receptor blockers after oral or intravenous dosing to determine whether smoking alters drug pharmacokinetics in a manner that could account for the earlier finding that smoking impairs therapeutic inhibition of nocturnal, but not pentagastrin-stimulated, gastric secretion.
Methods or Approach:
Gastric secretion was stimulated using a liquid meal containing a nonabsorbable marker to allow simultaneous measurement of gastric acid and pepsin secretion and transpyloric losses of gastric contents. Subjects, all habitual smokers, were examined twice after pretreatment i.v. with 200 mg cimetidine (smoking during one test and not the other) and twice with no pretreatment (same smoking restrictions). Plasma levels of ranitidine or cimetidine were measured in a separate group of subjects, twice after oral dosing together with food (smoking during one test and not the other) and twice after intravenous dosing (same smoking restrictions).
Results to Date:
Smoking did not alter gastric secretory output in response to food, either in inhibited or noninhibited stomach. However, smoking increased the volume of test meal emptied from the stomach by about 20 percent, and rate of delivery of acid and pepsin into the duodenum was similarly increased. Cigarette smoking increased rate of absorption of orally administered H_2-blockers, so that peak plasma levels were achieved sooner when smoking was permitted. After peak plasma levels had been achieved, for any given time, levels tended to be lower in subjects when they smoked, but elimination half-life and bioavailability were unchanged. The altered pharmacokinetics appear to be attributable to effects of smoking on gastric emptying, since smoking did not alter disposition of intravenously administered drugs. Findings may help explain loss of nocturnal inhibition with smoking, since breakthrough was maximal in the early hours of the morning, when differences in plasma drug levels caused by smoking would be most marked. However, this seems unlikely to account entirely for observed

loss of inhibition, and other mechanisms are being sought to explain the effects of smoking on inhibition of nocturnal gastric secretion.

Project Dates:
May 1983–May 1985.

Financial Support:
Dundee University; Glaxo Group Research, England.

0581. GLASGOW UNIVERSITY, RUCHILL HOSPITAL, Department of Community Medicine, Bilsland Drive, Glasgow G20 9NB, Scotland.

Project Title:
Evaluation of Breath Carbon Monoxide Measurements and Its Use as an Indicator of the Success of Antismoking Health Education.

Principal Investigators:
El-Gendawy, H.S.A.; Knill-Jones, R.P.; Hedley, A.J.

Objective:
To compare breath carbon monoxide measurements with blood carboxyhemoglobin measured by spectrophotometry and gas chromatography; use new portable carbon monoxide monitor to determine success of antismoking health education in hospitalized coronary heart disease patients.

Methods or Approach:
Patients admitted to the coronary care unit will be separated into smokers and nonsmokers. Smokers will be divided into two groups. Group 1 will receive routine health education; patients in group 2 will receive health education tailored specifically for individual conditions, based on physical and psychological findings, and dietary and smoking history.

Results to Date:
Data analysis in underway, but results are not yet available.

Project Dates:
June 1982–1985.

Financial Support:
Egyptian Government Scholarship.

0582. NINEWELLS HOSPITAL AND MEDICAL SCHOOL, Cardiovascular Epidemiology Unit, Dundee DD1 9SY, Scotland.

Project Title:
Scottish Heart Health Study Which Incorporates the Scottish Smoking Study.

Principal Investigators:
Tunstall-Pedoe, H.; Smith, W.C.; Crombie, I.K., et al.

Objective:
To (1) determine to what extent conventional coronary risk factors (cigarette smoking, blood pressure, serum cholesterol) explain variations in cardiovascular mortality in Scotland; (2) measure coronary risk factors in from 10,000 to 20,000 men and women; (3) conduct followup of subsequent mortality and cancer registration; (4) measure (in a subgroup) cigarette smoke metabolites (expired air carbon monoxide, serum thiocyanate, serum cotinine) and correlate levels with type and amount of tobacco smoked; and (5) relate results with morbidity and mortality.

Methods or Approach:
Men and women are selected from the Primary Care Administration (general practice list). In each locality, a random sample of 10 general practitioners is drawn and approached for permission to draw samples of patients (proportional to size of patient list). Questionnaires are mailed to each prospective patient requesting information on behavioral characteristics, symptoms, and smoking habits. Questionnaires are returned to a participating clinic and checked by a nurse. Blood pressure, weight and height, and expired air carbon monoxide are recorded, an electrocardiogram is made, and blood is drawn for analysis. A fat biopsy and a 24-hour urine collection are made.

Results to Date:
Project is in a preliminary phase.

Project Dates:
November 1984–1987.

Financial Support:
Scottish Home and Health Department; U.K. Department of Health and Social Security.

0583. NINEWELLS HOSPITAL AND MEDICAL SCHOOL, Cardiovascular Epidemiology Unit, Dundee DD1 9SY, Scotland.

Project Title:
Cigarette Smoking Behavior in School Children.

Principal Investigators:
Smith, W.C.S.; Fee, W.M.; Tunstall-Pedoe, H.

Objective:
To estimate prevalence of smoking; compare rates with previous studies in the same population using a carbon monoxide ecolyzer to validate history.

Methods or Approach:
The study cohort will include all third-year school children in the city of Dundee.

Results to Date:
Results are not yet available.

Future Plans:
Measurement of smoking behavior will be made in Scottish adult population with biochemical validation (carbon monoxide, thiocyanate, and cotinine) for the relationship with coronary heart disease.

Project Dates:
February 1984–February 1985.

0584. NINEWELLS HOSPITAL, UNIVERSITY MEDICAL SCHOOL, Department of Pharmacology and Clinical Pharmacology, Dundee, DD1 9SY, Scotland.

Project Title:
The Effects of Smoking on the Number and Properties of Nicotine and Serotonin Receptors in Human Brain.

Principal Investigators:
Balfour, D.J.K.; Benwell, M.E.M.; Anderson, J.M.

Objective:
To examine extent to which changes in brain nicotine receptors and serotonergic activity observed in rats treated chronically with nicotine can also be found in brains of human smokers.

Methods or Approach:
Postmortem material will be taken from brains of smokers and matched nonsmokers and homogenized to prepare membranes for receptor and enzyme studies. Effects of smoking on number and properties of 5-HT$_1$, 5-HT$_2$, and nicotine receptors and on tryptophan hydroxylase activity in discrete regions of the brain, notably the limbic system, will be examined.

Results to Date:
Preliminary studies have established that there are no rapid changes in the number of properties of the nicotine and 5-HT receptors present in brain tissue. Thus, biochemical investigation of these receptors in postmortem tissue appears to be a valid means of investigating effects of smoking on their properties.

Project Dates:
February 1984–January 1987.
Financial Support:
Scottish Home and Health Department.

0585. ROYAL INFIRMARY, Department of Respiratory Medicine, Glasgow G3, Scotland.

Project Title:
Smoking and Extrinsic Allergic Alveolitis (Hypersensitivity Pneumonitis).

Principal Investigators:
McSharry, C.; Boyd, A.
Objective:
To ascertain effect of smoking on incidence of extrinsic allergic alveolitis (hypersensitivity pneumonitis) among at-risk populations; determine effect of cigarette smoking on antibody production against inhaled antigens associated with extrinsic allergic alveolitis.
Methods or Approach:
Methods include (1) measurement of specific serum immunoglobulin G against relevant antigens by quantitative radioimmunoassay; (2) interviews of patients with alveolitis referred from chest clinics; and (3) interviews with at-risk patients including factory workers (where factory uses recirculating water air humidifier), pigeon breeders, and farm workers.
Results to Date:
Smokers have significantly reduced capacity to mount antibody response to inhaled antigens and also have reduced incidence of extrinsic allergic alveolitis.
Future Plans:
The effect of cigarette smoke on antibody response to inhaled antigens will be investigated in animals.
Project Dates:
1982–continuing.
Financial Support:
Western Infirmary, Glasgow; National Health Service.

0586. ROYAL INFIRMARY, Department of Medicine, Glasgow G31 2ER, Scotland.

Project Title:
The Effects of Acute Smoking on Platelet Behaviour, Fibrinolysis and Haemorheology in Habitual Smokers.

Principal Investigators:
Belch, J.J.F.; Forbes, C.D.
Objective:
To clarify mechanisms by which smoking may increase risk of arterial disease by studying platelet behavior, fibrinolysis, and hemorrheology in habitual smokers.
Methods or Approach:
Subjects (seven females and three males, average age 30 years) had smoked between 15 and 30 cigarettes/day for at least the previous 4 years. All had fasted overnight and none had smoked for at least 10 hours or taken any drugs that were known to affect laboratory tests for 2 weeks. Subjects smoked three cigarettes over a 30-minute period and blood was sampled before smoking and 10 min after the last cigarette. Blood was analyzed for platelet aggregation to 2 μg adenosine 5 diphosphate (ADP), plasma fibrinogen, plasminogen, plasminogen activator, α_2 macroglobulin antigen (α_2M), antithrombin III, factor VIIIc, β thromboglobulin, whole blood viscosity, plasma viscosity, red cell deformability, and white cell count.
Results to Date:
Results show that compared with age- and sex-matched controls, smokers had higher plasma fibrinogen ($p < 0.05$), lower plasminogen ($p < 0.02$) and plasminogen activator ($p < 0.05$), and higher plasma viscosity ($p < 0.003$). Changes seen in smokers after smoking three cigarettes were an increase in rate of platelet aggregation to ADP ($p < 0.02$), and an increase in α_2M ($p < 0.02$), and factor VIII RAG ($p < 0.05$). Plasma viscosity was decreased ($p < 0.02$), as was red cell deformability ($p < 0.02$). Findings confirm an increased tendency to hypercoagulability in smokers compared with nonsmokers, which becomes more pronounced immediately after smoking three cigarettes.
Future Plans:
The effect of smoking on prostaglandins and leukotrienes will be investigated.
Financial Support:
Royal Infirmary, Glasgow.
Reference:
Belch, J.J.F; McArdle, B.M.; Burns, P., et al. "The Effects of Acute Smoking on Platelet Behaviour, Fibrinolysis and Haemorheology in Habitual Smokers." *Thrombosis and Haemostasis* 51(1):6-8, February 28, 1984.

0587. UNIVERSITY MEDICAL SCHOOL, NINEWELLS HOSPITAL, Department of Pharmacology and Clinical Pharmacology, Dundee, DD1 9SY, Scotland.

Project Title:
Hippocampal 5-HT and the Effects of Nicotine in Stressed Rats.

Principal Investigators:
Balfour, D.J.K.; Vale, A.
Objective:
To investigate the role of hippocampal 5-HT systems in behavioral responses to nicotine, including effect in aversive environments; establish the mechanism by which nicotine modulates 5-HT systems in the hippocampus.
Methods or Approach:
The 5-HT innervation of the hippocampus will be lesioned selectively with 5,7-dihydroxytryptamine and the effects of the lesions on locomotor responses to nicotine will be examined using an elevated X-maze incorporating two open platforms as an aversive stimulus. Activity in the maze will be correlated to extent of lesioning produced and plasma corticosterone levels. Intracerebral injections into different parts of the brain will be used to attempt to find the site and determine the mechanism of action of the drug.
Results to Date:
Selective destruction of 5-HT pathways to the hippocampus causes a psychomotor stimulant effect similar to that seen in unlesioned animals given nicotine. Preliminary results suggest that lesions may enhance the antiaversive effects of nicotine and increase effects of nicotine withdrawal.
Project Dates:
January 1984–December 1986.
Financial Support:
MRC, United Kingdom.

0588. UNIVERSITY OF GLASGOW, RUCHILL HOSPITAL, Department of Community Medicine, Glasgow G20 9NB, Scotland.

Project Title:
Development of Reliable, Low Cost, Portable Measuring Devices for Measurement of Expired Air Carbon Monoxide.

Principal Investigators:
Gillies, P.M.; El-Gendawy, H.; Knill-Jones, R.P., et al.
Objective:
To develop and test portable low-cost carbon monoxide (CO) monitors for use in epidemiological and health promotion studies and for validation of survey data based on self-administered questionnaires.
Methods or Approach:
Low-cost eletrochemical cells are used as the basis for battery-powered portable units with LCD readout and audiovisual signals to indicate level of CO measured. Initial validation studies will include level of cross-sensitivity with H_2 and alcohol. Stability, precision, and coefficient of variation of readings will be estimated. Commercial development of the units is under consideration.
Results to Date:
Project is in a preliminary phase.
Future Plans:
Large-scale population-based surveys of high-risk groups in the West of Scotland will be conducted as part of a community smoking prevention program.
Project Dates:
September 1984–September 1986.
Financial Support:
Scottish Health Education Group, Health Education Council; University of Glasgow.

0589. UNIVERSITY OF GLASGOW, Department of Postgraduate Medical Education, Research Unit, 4 Lancaster Crescent, Glasgow G12 0RR, Scotland.

Project Title:
Health Education in the Primary School With Special Emphasis on the Prevention of Smoking.

Principal Investigators:
Calman, A.; Deans, G.; Carmichael, S., et al.
Objective:
To design, develop, and evaluate a health education program for upper primary school students aged 10 to 12 years to prevent smoking initiation.
Methods or Approach:
Preliminary research determined primary teachers' opinions about health and smoking education, which were taken into consideration in the design, approach, and content of the program. The program was evaluated in studies designed to determine its effect on attitudes and behavior of schoolchildren with regard to health in general and smoking in particular. The current project involves 2-year followup of smoking habits of two groups of children (1,200 each); one was taught the program and the other was not.
Results to Date:
The program is highly acceptable in terms of content and educational approach to both teachers and students. Results of early studies suggest that it does deter some children from trying cigarettes. One investigation involving 139 children who were taught the program and two untaught control cohorts (103 and 104 students, respectively) recorded a lower incidence of new cases of smoking experimentation among the treatment group compared with the control groups in the 2 years following intervention.
Project Dates:
September 1978–September 1985.
Financial Support:
Cancer Research Campaign, United Kingdom.

0590. WEST OF SCOTLAND CANCER SURVEILLANCE UNIT, Glasgow, Scotland. UNIVERSITY OF MICHIGAN, SCHOOL OF PUBLIC HEALTH, Ann Arbor, Michigan 48109.

Project Title:
Retrospective Case Control Study of Smoking Habits and Lung Cancer in the West of Scotland.

Principal Investigators:
Gillis, C.R.; Hole, D.J.; Hawthorne, V.M., et al.
Objective:
To study smoking habits and the tar content of cigarettes smoked in relationship to incidence and mortality from lung cancer; compare this with a prospective cohort study carried out in the same part of Western Scotland.
Methods or Approach:
A retrospective case–control study and a cohort study were utilized in the investigation.
Results to Date:
A possible flattening in the dose–response was found and a low relative risk in an area of the world with one of the highest recorded incidences of lung cancer. The flattening of the dose–response curve occurred with an above-average consumption of 20 cigarettes/day.
Future Plans:
Followup will be continued by record linkage and specific studies, and comparison with other countries will be made.
Project Dates:
September 1976–May 1981.
Financial Support:
NIH (N01-CP-05646); West of Scotland Cancer Surveillance Unit; King Edward VII Memorial Fund; Scottish Home and Health Department.

0591. WEST OF SCOTLAND CANCER SURVEILLANCE UNIT, RUCHILL HOSPITAL, Glasgow, Scotland.

Project Title:
Health Effects of Exposure to Environmental Tobacco Smoke in the West of Scotland.

Principal Investigators:
Gillis, C.R.; Hole, D.J.; Hawthorne, V.M.
Objective:
To establish prevalence of self-reported respiratory and cardiovascular symptoms, together with FEV levels, in categories of individuals with increasing exposure to environmental tobacco smoke; study mortality and cancer incidence experience of those individuals with increased exposure to environmental tobacco smoke, with particular attention to lung cancer and other smoking-related parameters.
Methods or Approach:
A cohort of 16,171 apparently healthy individuals aged 45 to 64 years residing within a defined geographical area in western Scotland were screened for cardiorespiratory disease between 1972 and 1976. Members of the same household attended the screening unit, so smoking and nonsmoking partners of smokers and nonsmokers have been linked and categories defined to represent increasing exposure to environmental tobacco smoke. Long-term followup for subsequent cancer incidence and all-cause mortality has been effected using the appropriate national data sources.
Results to Date:
Prevalence of self-reported respiratory symptoms is approximately 40 percent higher in nonsmokers with a smoking partner than in nonsmokers with a nonsmoking partner. This is

consistent for males and females. No difference in prevalence of cardiovascular symptoms was found. Short-term followup of lung cancer and smoking-related mortality suggests a slightly raised level in those exposed to environmental tobacco smoke.

Future Plans:

Followup of cancer incidence and mortality will continue and methods will be examined whereby exposure to environmental tobacco smoke might be quantified.

Project Dates:

March 1980–continuing.

Financial Support:

West of Scotland Cancer Surveillance Unit.

0592. WESTERN GENERAL HOSPITAL, INFERTILITY CLINIC, University Department of Surgery/Urology, Edinburgh, Scotland.

Project Title:

Cigarette Smoking and Male Infertility.

Principal Investigator:

Hargreave, T B

Objective:

To gather epidemiological evidence about the impact of cigarette smoking in couples who complain of infertile marriage.

Methods or Approach:

This is a continuation of previous projects that examined the impact of cigarette smoking on sperm structure. For the last 5 years, detailed smoking histories have been obtained from all couples attending the infertility clinic. Information has been recorded prospectively on computerized files. Data will be analyzed in relation to subsequent pregnancy rates, and searched for interaction between cigarette smoking and other factors that cause male infertility.

Results to Date:

To date, results have been conflicting. In investigating morphology of sperm, examined by light microscopy, a significant increase in number of abnormal morphological forms were found in patients who smoked compared with those who did not smoke. A second study, using scanning electron microscopy, found no difference in sperm morphology in smokers compared with nonsmokers, although there were differences in fertile patients compared with infertile patients. A possible explanation is that the features measured with the two different systems are different.

Future Plans:

An epidemiological analysis will be carried out in 1985.

Project Dates:

March 1978–March 1988.

References:

(1) Evans, H.J.; Fletcher, J.; Torrance, M., et al. "Sperm Abnormalities and Cigarette Smoking." *Lancet* 1(8221):627-629, March 21, 1981. (2) Hol.as, S.; Willams, A.; Tocher, J.L., et al. "Scoring Sperm Morphology From Fertile and Infertile Cigarette Smokers Using the Scanning Electron Microscope and Image Analysis." *Fertility and Sterility* (Accepted for publication).

Wales.

0593. BRITISH THORACIC SOCIETY, SULLY HOSPITAL, Sully, Nr. Penarth, South Glamorgan CF6 2YA, Wales.

Project Title:

A Study of Four Methods of Achieving Smoking Withdrawal in a Population of Hospital In-Patients and Out-Patients With Smoking Related Diseases.

Principal Investigator:

Campbell, I A

Objective:

To compare four methods of smoking withdrawal in patients with smoking-related diseases.

Methods or Approach:

The multicenter study compared effects of (1) verbal advice from the physician and instructions to stop smoking; (2) addition of an information booklet about the dangers of smoking and advice on how to quit; (3) addition of placebo chewing gum to substitute for cigarettes when the urge to smoke arises; and (4) addition of 2 mg nicotine chewing gum instead of placebo. Treatments were allocated in random order. Physicians initially received 12 envelopes and 6 containers of gum marked A, B, C, or D. In addition to the treatment allocation notice, each envelope contained an entry card and patient's questionnaire; nine envelopes also contained the smoking withdrawal advice leaflet. Three containers held active gum and three placebo gum, assuming use of 10 to 15 pieces of gum/day over a 3-month period, divided into 1-month and 2-month supplies within each container. Participants were patients with smoking-related diseases who agreed to try to quit. Followup was at 1, 3, 6, and 12 months after entering the study. At 1-month visit, patients in the chewing gum groups received a further 2 months' supply of gum. At 3 months, further supplies were offered only if patients felt it necessary. No further supplies of gum were issued. Patients claiming to have stopped smoking at 6 months and 12 months were tested for carboxyhemoglobin and thiocyanate.

Results to Date:

At 1-year followup, none of the other methods tested gave better results than verbal advice from the physician. Chewing gum clearly aided abstinence at 1 month and at 3 months, but there were no significant differences between active and placebo gum. At 6 months, the superiority of chewing gum had disappeared. This remained true at 12 months, with active and placebo preparations again having similar effects. Overall, 9.7 percent of 1,550 patients had successfully quit smoking.

Project Dates:

January 1980–December 1982.

Financial Support:

Health Education Council, London.

0594. BRITISH THORACIC SOCIETY, SULLY HOSPITAL, Sully, Nr. Penarth, South Glamorgan CF5 2YA Wales.

Project Title:

The British Thoracic Society's Second Smoking Withdrawal Study: Physicians' Usual Advice vs. That Advice Reinforced by Health Visitors and by Postal Encouragement.

Principal Investigator:

Campbell, I A

Objective:
To compare effects of usual advice from the physician about smoking and verbal instruction to stop with the effects of the addition of a specific date for stopping within the next 7 days, a signed agreement to try to stop smoking, and written and personal contact (Health Visitor) to reinforce initial advice.
Methods or Approach:
New clinic patients with smoking-related diseases are advised by the physician to stop smoking and randomly allocated to one of two groups. Group 1 patients are given appointments for 6 months later. Those who are nonsmokers at 6 months are given a further appointment in 6 months. Patients in group 2 are asked to sign an agreement to try to stop smoking. In a few days, they receive a reminder from the physician about stopping. The physician then arranges for a Health Visitor to call on the patient at 2 and 6 weeks following initial consultation to reinforce the advice. At 2, 3, and 5 months, the physician sends a (preprinted) encouraging letter to the patient. The 5-month letter mentions that the patient will be seen in the outpatient clinic in a month's time. At 6 months, patients who are nonsmokers are given a further appointment at 6 months, and at 9 months are sent a letter of encouragement. Carboxyhemoglobin is measured in those who claim to have stopped smoking.
Results to Date:
Project is in a preliminary phase.
Project Dates:
October 1984–September 1987.
Financial Support:
Cancer Research Campaign, London.

0595. CARDIFF ROYAL INFIRMARY, Dialysis Unit, Cardiff CF2 1SZ, Wales.

Project Title:
Effects of Smoking on A/V Fistula Patency.

Principal Investigators:
Griffin, P.J.A.; Davies, F.
Objective:
To assess effects of smoking, hematocrit, and plasma lipids on short- and long-term patency of arteriovenous (A/V) fistulae used in renal dialysis.
Methods or Approach:
Questionnaires are completed by patients on smoking habits, and hematocrit and lipids are measured at time of fistula construction.
Results to Date:
Data show a significantly greater incidence of long-term fistula failure in smokers.
Future Plans:
The combined effects of smoking, hematocrit, and plasma lipids will be assessed prospectively.
Project Dates:
June 1982–December 1985.
Financial Support:
Cardiff Royal Infirmary.
Reference:
Griffin, P.J.A.; Davies, F., Salaman, J.R., et al. "Effects of Smoking on Long Term Patency of Arteriovenous Fistulas." *British Medical Journal* 286(6366):685-686, February 26, 1983.

0596. HEARTBEAT WALES, 24 Park Place, Cardiff, Wales. UNIVERSITY OF SOUTHAMPTON, Southampton, England.

Project Title:
Development of Smoking Among Children. Effects of Transfer From Primary to Secondary Education.

Principal Investigator:
Nutbeam, D.
Objective:
To (1) identify effect of transition from primary to secondary school on development of smoking habit; (2) investigate contributory factors to any changes in prevalence; and (3) suggest remedial action.
Methods or Approach:
Self-administered questionnaires were completed by a cross section of 4,000 children in years immediately before and after transfer in three different school systems with a different age of transfer. Effects of transfer could thus be isolated from effects of chronological age. A 2 percent subsample of all children was subsequently interviewed about experiences during transfer and any influences on behavior.
Results to Date:
Data provide good evidence that transition from primary to secondary school does affect development of smoking independently of chronological age. Explanations by students during interviews included social factors (exposure to older children), school factors (apparent tolerant attitude toward smoking in secondary schools), and individual factors (boost to self-esteem).
Future Plans:
Work will be continued in experimental schools to examine practical strategies for helping children overcome some of the negative effects of school transfer.
Project Dates:
September 1983–September 1986.
Financial Support:
Heartbeat Wales; Health Education Council, United Kingdom.

0597. HEARTBEAT WALES, 24 Park Place, Cardiff, Wales. UNIVERSITY OF SOUTHHAMPTON, Southampton, England.

Project Title:
Investigation of Teachers' Smoking Behavior and Attitudes to Smoking.

Principal Investigator:
Nutbeam, D.
Objective:
To identify differences in smoking behavior and attitudes toward smoking among primary and secondary schoolteachers; determine differences in attitudes toward smoking in smokers and nonsmokers.
Methods or Approach:
An invitation was sent to 500 teachers in 30 primary and secondary schools to complete a self-administered questionnaire; 80 percent responded.
Results to Date:
Data are being analyzed; results will be available in May 1985.
Project Dates:
September 1983–September 1985.
Financial Support:
Heartbeat Wales; Health Education Council, United Kingdom.

0598. MEDICAL RESEARCH COUNCIL, Epidemiology Unit, 4 Richmond Road, Cardiff CF2 3AS, Wales.

Project Title:
Caerphilly Prospective Study of Ischemic Heart Disease.

Principal Investigators:
Yarnell, J.W.G.; Elwood, P.C.; Sweetnam, P.M.
Objective:
To study determinants of ischemic heart disease (IHD) in a population of men and women from Caerphilly, South Wales.
Methods or Approach:
A cohort study of 2,400 men aged 44 to 60 years began in 1979 in Caephilly, South Wales. Major emphasis is placed on possible hemostatic and dietary determinants of IHD. Seven-day weighed dietary records have been obtained in the entry phase on a 1:3 subsample of subjects. Two samples of women have also been studied.
Results to Date:
Preliminary data indicate a high prevalence of IHD in South Wales. A significant association between white cell count and IHD defined cross-sectionally is not explained by smoking habits. prevalent ischemic heart disease is not explained by smoking habit in a preliminary analysis of the data.
Project Dates:
September 1979–1987.
Financial Support:
MRC, United Kingdom.

0599. ROYAL GWENT HOSPITAL, CORONARY CARE UNIT, Newport, Gwent, Wales.

Project Title:
Education of Post-Infarction Patients by Nurses.

Principal Investigators:
Jenkins, B.; Mayberry, J.; Kent, S., et al.
Objective:
To assess value and efficiency of health education given by nurses, especially in reduction of smoking.
Methods or Approach:
Patients are identified by electrocardiogram and enzyme changes. Education is provided by nurses and followup is conducted by questionnaire and interview.
Results to Date:
Patients want further education on healthy living and appear to reduce smoking following the nurse's program.
Project Dates:
August 1981–September 1983.

0600. SULLY HOSPITAL, Sully, Nr. Penarth, South Glamorgan CF6 2YA, Wales.

Project Title:
General Practitioner Study of Nicotine Chewing Gum in the Cardiff Area of South Wales.

Principal Investigators:
Campbell, I.A.; Lyons, E.; Prescott, R.J.
Objective:
To (1) compare effects of nicotine and placebo chewing gum in smokers visiting their general practitioner; (2) compare effect of a letter sent at 1 month with/without followup warning; and (3) analyze sex, age, occupation, and diagnosis for any effect on success or failure.
Methods or Approach:
Subjects (870 cigarette smokers), who had been advised to quit smoking by the physician and had agreed to try, were allocated in a random manner to either placebo or nicotine chewing gum. Participants were given a 6-week supply of gum, assuming consumption of 15 pieces/day, and a leaflet explaining use of the gum. Patient's name, sex, address, age, occupation, diagnosis (if any), and number of cigarettes smoked/day were recorded. A month later, a letter was sent to two-thirds of the patients reminding them to quit; half of the letters also mentioned that inquiry would be made at 12 months concerning smoking. At 12 months, all patients were contacted by mail and asked about smoking. Those claiming to have quit were tested for carbon monoxide in expired air. A nonintervention group of 152 patients were also contacted at 12 months and asked if they had stopped smoking.
Results to Date:
Results are not yet available.
Project Dates:
June 1983–December 1984.
Financial Support:
Chest, Heart and Stroke Association, London.

0601. UNIVERSITY HOSPITAL OF WALES, UNIVERSITY COLLEGE OF MEDICINE, Department of Medicine, Heath Park, Cardiff CF4 4XN, Wales.

Project Title:
Cardiorespiratory Response to Exercise Before and After Beta Adrenoreceptor Blockade in Nonsmokers and Chronic Smokers.

Principal Investigators:
Penny, W.J.; Mir, M.A.
Objective:
To investigate chronic effects of cigarette smoking on heart rate and oxygen consumption during exercise and on effects of beta blockade before and after exercise in young healthy smokers and nonsmokers.
Methods or Approach:
Exercise is on an exercise bicycle (ergometer); oxygen consumption is measured by a portable instrument oxylog. Propranolol/placebo is given intravenously and an exercise electrocardiograph is monitored continuously.
Results to Date:
Resting heart rate in smokers is significantly higher than in nonsmokers (75 beats/min vs. 64 beats/min). During exercise, heart rate remains significantly higher in smokers and smokers have higher oxygen consumption. Beta blockade reduces exercise tachycardia in both groups, but heart rate for the same work load remains significantly higher in smokers.
Future Plans:
Similar studies will be conducted among smokers and nonsmokers with ischemic heart disease and studies will be repeated in patients who give up smoking to evaluate residual effect of chronic smoking.
Project Dates:
April 1981–April 1985.

0602. UNIVERSITY OF WALES, COLLEGE OF MEDICINE, Department of Medicine, Cardiff CF4 4XN, Wales.

Project Title:
Interaction Between Haematocrit, Haemoglobin and Oxygen Saturation in Healthy Smokers and Nonsmokers.

Principal Investigators:
Tirlapur, V.G.; Mir, M.A.
Objective:
To investigate the interaction between smoking habits, age, sex.

hemoglobin concentration, hematocrit, and arterial oxygen saturation in healthy subjectsest

Methods or Approach:
Hemoglobin is measured by Cyn-Met (model S) and hematocrit is calculated by a Coulter counterest Oxygen saturation is measured by an ear oximeter (Hewlett Packard 47201A).

Results to Date:
Hemoglobin concentrations were higher in female heavy smokers aged 40 to 59, and in both sexes, in light smokers over the age of 60 than in nonsmoking counterparts. Oxygen saturation was lower in male heavy smokers aged 20 to 39 years and in older female light smokers. Results show that changes in oxygen saturation are seen at a younger age than changes in hemoglobin concentration and hematocrit.

Future Plans:
Effect of withdrawal from smoking on hematocrit, hemoglobin concentration, and oxygen saturation will be studied in various age groups. Long-term followup studies will observe differences in parameters in continued abstainers and recidivists.

Project Dates:
April 1981–September 1987.

Financial Support:
University of Wales.

UNITED STATES

Alabama

0603. AGRICULTURAL RESEARCH SERVICE, Auburn, Alabama 36830.

Project Title:
Bioassay of Deproteinized and Other Experimental Cigarettes.

Principal Investigators:
Tso, T.C.; Bock, F.G.

Objective:
To determine and compare the possible carcinogenicity of experimental cigarettes with or without removal of soluble proteins.

Methods or Approach:
Experimental cigarettes made of two types of tobaccos, either conventionally cured or homogenized leaf cured, with or without removal of soluble proteins, will be used for bioassay. Four bright samples will be bioassayed by both long-term skin painting and sebaceous gland suppression, and four burley samples will be bioassayed by sebaceous gland suppression for evaluation and comparison of possible carcinogenicity differences resulting from those treatments.

Results to Date:
Bioassay of these groups of samples are now complete. In the determination of sebaceous gland suppression activity, maleic hydrazide (MH) spiked sample (1000 ppm) did not differ significantly in suppression activity among MH normal level treatment and others, although MH treatment resulted in a higher activity than control. Bright conventional curing control had a higher activity than HLC or reconstituted sheets. Tobacco of close-spacing HLC with stalk, plus removal of Po^{210} and protein is least active, and in burley samples, different nicotine levels showed no significant effects on activity. In the determination of carcinogenic activity, long-term skin painting results showed that tobacco spiked with 1000 ppm MH is more active than others; field-treated is less active than control close-spacing, and removal of Po^{210} reduced activity. Cigarettes made with reconstituted stalk is less active, and leaves for lower stalk positions yield condensate more active than those from upper portions. The HLC samples with or without protein removal were not sufficient for complete long-term skin painting. The results, therefore, cannot be evaluated statistically.

Project Dates:
May 1978–March 1982.

Financial Support:
USDA (1090-20831-007-C).

Reference:
Bock, F.G. "Cocarcinogenic Properties of Nicotine." In: Gori, G.B.; Bock, F.G. (Editors). *Banbury Report 3: A Safe Cigarette?* Cold Spring Harbor, New York, Cold Spring Harbor Laboratory, 1980, pp. 129-140.

0604. AUBURN UNIVERSITY, Auburn, Alabama 36830.

Project Title:
Vitamin C and Acute Physiological Responses to Cigarette Smoking.

Principal Investigator:
Keith, R.E.

Objective:
To (1) determine effects of a single vitamin C supplement on the acute effects of cigarette smoking; (2) determine optimum vitamin C dose–response level germane to acute effects of cigarette smoking; and (3) determine effects of long-term vitamin C diet supplementation on acute effects of cigarette smoking.

Methods or Approach:
Heart rate, blood pressure, and various lung function test values were recorded on rested cigarette-smoking subjects before and after smoking two cigarettes. Data were recorded 4 hours before and after subjects consumed a single oral dose of vitamin C or a placebo, and after subjects consumed vitamin C or the placebo for 2 weeks.

Results to Date:
Results have been published.

Project Dates:
January 1979–September 1982.

Financial Support:
USDA (ALA00493).

References:
(1) Keith, R.E.; Merrill, E. "The Effects of Vitamin C on Maximum Grip Strength and Muscular Endurance." *Journal of Sports Medicine and Physical Fitness*, 1983. (2) Keith, R.E.; Mossholder, S.B. "Vitamin C and Acute Physiological Responses to Cigarette Smoking" *Nutrition Research* 3:653-661, 1983. (3) Mossholder, S.B.; Keith, R.E. "Ascorbic Acid Status of Smoking and Nonsmoking Adolescent Females." *Federation Proceedings* 42(4):1065, 1983.

0605. UNIVERSITY OF ALABAMA AT BIRMINGHAM, Division of General and Preventive Medicine, 1717 11th Avenue, S., Birmingham, Alabama 35205.

Project Title:
A Multidisciplinary Program for Intervention for Hypertension and Smoking Cessation.

Principal Investigators:
Hataway, C.J.; Maisiak, R.C.
Objective:
To develop and implement a model protocol program for the physician and staff personnel in primary care practice to detect, evaluate, treat, and follow any patient with elevated blood pressure or currently smoking cigarettes.
Methods or Approach:
The first 6 months were devoted to development and completion of all educational and testing materials. The refined model of the program was implemented among a group of 25 physician participants and assessment was made. Final analyses were conducted and the program was presented to practitioners throughout Alabama.
Results to Date:
The model program provides effective smoking cessation techniques for all community physicians to use with patients who smoke.
Future Plans:
It is anticipated that findings will be published.
Project Dates:
December 1981–April 1985.
Financial Support:
Robert Wood Johnson Foundation.

0606. UNIVERSITY OF ALABAMA AT BIRMINGHAM, Department of Nutrition Sciences, University Station, Birmingham, Alabama 35294.

Project Title:
Localized B_{12}:Folate Deficiency and Lung Cancer in Smokers.

Principal Investigators:
Krumdieck, C.L.; Butterworth, C.E., Jr.; Heimburger, D.C., et al.
Objective:
To determine whether exposure to cigarette smoke results in a localized B_{12} and folate deficiency, manifested primarily in the bronchial epithelium, that renders it more susceptible to neoplastic transformation by the carcinogenic hydrocarbons of tobacco smoke.
Methods or Approach:
Components of tobacco smoke (i.e., organic nitrites, nitrous oxide, cyanates, and cyanides) are known to attack some forms of B_{12} and folate coenzymes, transforming them into biologically inactive compounds. The presence of megaloblastic changes indicative of B_{12} or folate deficiency in the bronchial epithelium of chronic smokers is being investigated in sputum cytology specimens and in bronchial and carinal biopsy specimens. The reaction of certain components of tobacco smoke with B_{12} and tetrahydro folates is being investigated in vitro. Formation of biologically inactive derivatives is tested by bioassays and spectroscopic studies. Smokers with metaplasia (by sputum cytology) are being given a supplement of B_{12} and folic acid in a double-blind design and evolution of preneoplastic lesions is being followed by repeated cytologic examination.
Results to Date:
B_{12} and folate cofactors react in vitro with organic nitrites (butyl nitrite used as model compound) to form biologically inactive derivatives. Chronic smokers (≥ 20 pack-years) have significantly lower plasma and red blood cell folates than nonsmokers, and smokers with metaplasia have lower plasma folates than smokers without metaplasia. B_{12} levels (by radioisotope dilution) are not significantly different in nonsmokers and smokers with/without metaplasia. There is a trend toward lower vitamin C plasma levels in smokers with metaplasia, but no differences were observed for B_1, B_2, B_6, A, carotene, or E vitamins. Results of the double-blind study are not yet available.
Project Dates:
September 1983–August 1986.
Financial Support:
NCI (CA34275-02).

0607. UNIVERSITY OF ALABAMA IN BIRMINGHAM, SCHOOL OF PUBLIC HEALTH, 209 Tidwell Hall, Birmingham, Alabama 35294.

Project Title:
Smoking Cessation Programs for University Employees.

Principal Investigators:
Windsor, R.A.; Bartlett, E.E.; Lowe, J.B.
Objective:
To (1) establish smoking prevalence and trends for University of Alabama employees by surveying the smoking history and habits among a random sample of full-time employees every 6 months for a 3-year period; (2) refine and implement the three components of the multicomponent, self-guided smoking cessation program for university employees; and (3) determine the individual and combined effects of three self-guided smoking cessation modalities.
Methods or Approach:
Three multicomponent interventions have been created and are being evaluated through the use of a randomized pretest–posttest control group, 2 x 2 factorial design. The interventions are (1) the American Lung Association's "Freedom From Smoking" self-help manual; (2) commitment enhancement, social support, and health education skills training; and (3) monetary incentive. During the 3-year project, 400 smokers will be recruited from the employee population and information will be gathered at baseline, 6 weeks, 6 months, and 12 months for each employee. In addition, saliva thiocyanate will be used to validate self-reports of smoking/smoking cessation.
Results to Date:
Preliminary information indicates that approximately 21 to 25 percent of university employees smoke cigarettes. Information on cessation rates is not yet available.
Project Dates:
September 1983–August 1986.
Financial Support:
NHLBI (HL 30630-02).

0608. UNIVERSITY OF ALABAMA IN BIRMINGHAM, Department of Medicine, 700 19th Street, S., Birmingham, Alabama 35233. VETERANS ADMINISTRATION MEDICAL CENTER, Birmingham, Alabama 35233.

Project Title:
Altered Platelet Aggregation Following Acute Myocardial Infarction.

Principal Investigator:
McDaniel, H.G.
Objective:
To (1) determine the course of platelet aggregation following myocardial infarction (MI); (2) examine the influence of

smoking, diabetes, and sex on alteration of platelet function found in patients after myocardial infarction; (3) identify plasma factors that alter platelet aggregation and thromboxane B_2 production from arachidonic acid after MI; and (4) correlate data with the clinical course of the patient, mode of therapy used, and presence or absence of coronary artery spasm.

Methods or Approach:

Platelet aggregation is measured in fresh platelets serially drawn over several days after MI in hospitalized patients. Aggregation is induced by adding 0.5 mmol arachidonic acid. Thromboxane B_2 production is measured by radioimmunoassay. Plasma prostaglandin 6-keto $F_{1\alpha}$ levels are also measured by radioimmunoassay. Plasma that actively inhibits platelet aggregation is being fractionated by silic acid chromatography to identify the plasma factor that inhibits platelet aggregation.

Results to Date:

The first 48 hours after MI, platelet aggregation and thromboxane B_2 production from arachidonic acid is markedly decreased, owing to a plasma factor that appears to be a polar lipid, since it is extracted from whole plasma by organic solvents and is retained on a silic acid column.

Future Plans:

Gas chromatography-mass spectroscopy and immunologic and chromatographic techniques will be used to identify the plasma factor. Serial plasma levels will be followed and correlated with the clinical course of patients and various risk factors and modes of therapy.

Project Dates:

January 1980–January 1986.

Financial Support:

University of Alabama in Birmingham; VA; NHLBI (HL 17667).

0609. UNIVERSITY OF ALABAMA, Department of Microbiology, Box BM, University, Alabama 35486.

Project Title:

Interferon Induction in the Human Population; Effects of Smoking, Chronic Disease and Cancer.

Principal Investigators:

Winters, A.; Frankel, J.W.

Objective:

To evaluate the relationship between poly I–poly C-induced interferon (IFN) titers and Kirsten murine sarcoma (KiMSV) titers from cancer patients and controls.

Methods or Approach:

Skin fibroblast cell cultures were developed from punch biopsies (28 male lung cancer patients and 34 male controls) and foreskins (51 newborns). Adults were from 47 to 72 years of age. All cancer patients had an extended smoking history and had received chemotherapy and/or radiation. The reciprocal of the highest tenfold KiMSV dilution that induced a focus of transformed cells in one of duplicate flasks was recorded as the endpoint. Interferon titers in cultures derived from the same donor were measured after a poly I–poly C-superinduction with cycloheximide and actinomycin.

Results to Date:

An inverse relationship between KiMSV transforming titers and induced IFN titers was observed and confirmed by statistical analysis of the strength of association ($p < 0.002$). A relatively large degree of variability with respect to induced IFN titers was observed in cancer, control, and newborn populations, an observation reported previously with newborns. Median IFN titers of cancer patients and controls (20 and 160, respectively) were significantly different ($p < 0.01$).

Future Plans:

The role of chemotherapy and radiation in the phenomenon of decreased ability to respond to IFN induction will be assessed by examining IFN induction in skin fibroblast cultures derived from skin snips obtained at closing of thoracic surgery for removal of lung tumors (prior to initiation of antitumor treatment).

Project Dates:

December 1980–June 1983.

Financial Support:

CTR.

0610. UNIVERSITY OF ALABAMA, BIRMINGHAM, 720 20th Street, S., Birmingham, Alabama 35294.

Project Title:

Small for Gestational Age Births.

Principal Investigator:

Goldenberg, R.L.

Objective:

To conduct a longitudinal study of fetal growth and perinatal outcome of women at risk for delivering small for gestational age (SGA) infants.

Methods or Approach:

Multiparous women at risk for SGA births will be identified (n = 1,500), and pregnancies will be followed and documented. A data base will be created that will include information on sociodemographic, nutritional, and lifestyle characteristics and on medical aspects of the prenatal, labor and delivery, and newborn and infant periods. Data on smoking habits will be available on all participants.

Results to Date:

Project is in a preliminary phase.

Project Dates:

June 1984–May 1989.

Financial Support:

NICHD (N01HD42811).

0611. UNIVERSITY OF ALABAMA, BIRMINGHAM, SCHOOL OF NURSING, University Station, Birmingham, Alabama 35294.

Project Title:

Teenage Smoking Behavior Related to the Availability of Smoking Areas on School Grounds.

Principal Investigator:

Crow, C.S.

Objective:

To add to the general body of knowledge about factors that either initiate smoking or favor its continuation among teenagers.

Methods or Approach:

Using a descriptive comparative design, a short questionnaire was administered to the target population and matched controls. Surveys were conducted at two suburban high schools similar in size and socioeconomic status, near a southern metropolitan area. One school provided a smoking area for students who smoke. Data were analyzed and described in terms of frequency of response (N), relative frequencies (percent), and Chi-square or t-test where appropriate.

Results to Date:

By the definition used for a smoker, 24.7 percent of adolescent subjects smoked, which appears to be consistent with national figures when adjusted for age differences in various studies and for variations in the definition of a smoker. There were more smokers at the school that had a designated smoking area (33 percent) than at the school without a designated area (20 percent). There was also a significant relationship between the incidence of cigarette smoking among high school students and provision of a student smoking area ($p<0.05$). Findings suggest that providing a smoking area for students increases incidence of adolescent smoking. Fifty-eight percent of the smokers were females. Comparing the number of female vs. male smokers with other studies, it appears that female adolescent smoking may be stabilizing at about 14 percent, while the rate among male adolescents may be decreasing. The overall rate was 10.4 percent for male smokers compared with a rate of 14 to 15 percent in other studies. The mean number of cigarettes smoked/day was 12.3. Additional research is needed before a clear conclusion can be drawn; however, for educators and professionals, the question remains as to whether a school that provides a student smoking area is encouraging adolescents to smoke.

0612. UNIVERSITY OF SOUTH ALABAMA, COLLEGE OF MEDICINE, **Department of Pharmacology, MSB Room 3130, Mobile, Alabama 36688.**

Project Title:
Studies of Platelet and Endothelial Prostanoid Production as Possible Cardiovascular Risk Indicators in Smokers. Effects of Smoking and Nicotine on Arachidonic Acid Metabolism of Human Platelets and Vascular Endothelium.

Principal Investigator:
Longenecker, G.L.

Objective:
To determine the effects of smoking and nicotine on the relative levels of platelet regulatory prostanoids thromboxane A_2 and prostacyclin, and on the relative proportion of arachidonic acid metabolized through the cyclooxygenase and lipoxygenase pathways.

Methods or Approach:
Smokers and nonsmokers (divided into males and females under and over age 35) underwent three independent venipunctures before, during, and 60 minutes after smoking (or match-time) to determine levels of thromboxane A_2 and prostacyclin metabolites TxB_2 and 6-O-PGF$_{1\alpha}$, respectively, in serum (untreated or indomethacin-treated blood) by radioimmunoassay (RIA). Platelet aggregometry was performed at the same times, using a portion of the blood, which was immediately citrated to prepare platelet rich plasma (PRP) by low speed, room temperature centrifugation. PRP dose–responses to ADP, epinephrine, arachidonic acid, and collagen were determined. Standard hematologic parameters were also determined (platelet count, white cell count, hematocrit, hemoglobin, red cell count). Several nested pilot studies determined total releasable beta-thromboglobulin by RIA, number of α_2 adrenergic receptors (yohimbine binding), and effects on platelet aggregability and on cultured endothelial cell release of prostacyclin of nicotine, benzo(*a*)pyrene (BaP), and carbon monoxide. Additional studies will include effects of smoking and nicotine on lipoxygenase(s)/lipoxygenase products and chronic effects of nicotine on arachidonate metabolism of platelets and endothelium.

Results to Date:
Significant differences in RIA levels of 6-O-PGF$_{1\alpha}$ existed by age and sex group but differences between smokers and nonsmokers could be demonstrated (at the $p=0.07$ level) only for the 60 minutes postsmoking sample, when nonsmokers undergo a decline in levels and smokers an elevation. Basal levels of TxB_2 in indomethacin-treated blood showed differences for sex group and smoking, while TxB_2 released by endogenous thrombin stimulation of platelets (untreated blood) showed an effect of age with little influence by sex group or smoking. Platelet counts were higher in smokers, and platelets were slightly more responsive to aggregation by all agents tested in the before-smoking sample and returned to near normal by the 60 minutes postsmoking sample. The change in epinephrine responsiveness was particularly striking, with about twice as many smokers as nonsmokers losing the second phase of aggregation altogether, which may be related to an increased number of α_2 receptors on the platelets of smokers (demonstrated as increased yohimbine binding). Nicotine was found to have little effect on platelet aggregability, but could either decrease or increase 6-O-PGF$_{1\alpha}$ release by cultured endothelial cells. BaP was found to stimulate endothelial cell release of 6-O-PGF$_{1\alpha}$ and to alter platelet aggregation responses, with the latter being multiphasic (inhibition-stimulation-inhibition). Carbon monoxide increased endothelial cell release of 6-O-PGF$_{1\alpha}$, but was not tested for effect on platelets. It is anticipated that smoking and nicotine exposure will increase lipoxygenase products, and that acute and chronic in vitro effects of nicotine on cultured endothelium will differ, perhaps by "accommodation."

Project Dates:
July 1981–June 1984.

Financial Support:
CTR.

0613. UNIVERSITY OF SOUTH ALABAMA, COLLEGE OF MEDICINE, **Department of Pharmacology, MSB Room 3130, Mobile, Alabama 36688.**

Project Title:
Nicotine and Human Endothelium-Platelet-Tumor Cell Interactions.

Principal Investigator:
Longenecker, G.L.

Objective:
To determine the effect of nicotine on aggregation of platelets by tumor cells and on adhesion of platelet-tumor cell aggregates to endothelium, processes that may be important to occurrence of metastasis.

Methods or Approach:
Platelet rich plasma (PRP) derived from freshly drawn heparinized human blood by low-speed room temperature centrifugation is used to test aggregation-inducing ability of tumor cells (suspensions of known density derived from monolayers in culture without proteases). Tumor cell types used include rhabdosarcoma (RD), cervical adenocarcinoma (HeLa), and prostatic adenocarcinoma (PC-3). Other types, particularly lung tumor cells, will also be used. Nicotine is added either to the tumor cells or to PRP prior to addition of tumor cells to PRP, and rate and maximum achieved aggregation response is determined and compared with a corresponding no-treatment control. The effect of nicotine on adhesion of tumor cells, platelets, or tumor cell-platelet aggregates to endothelium or of platelets to tumor cells is assessed by adding fixed count suspension of test cells (or labeled test cells) to confluent monolayers of human endothelium derived from umbilical vein, with withdrawal of aliquots for particle counting and/or removal of suspension and scintillation counting of label subsequent to washing and removal of cells from their support. Supernatant from all systems may be analyzed for production/changes in production of arachidonic acid metabolites via high pressure liquid chromatography/radioimmunoassay/mass spectroscopy, as available/appropriate.

Results to Date:
Nicotine (10 to 100 M) increases the rate and maximum aggregation response of PRP to both RD and PC-3 cells. In addition, nicotine increases adhesion of platelets to RD cells or HeLa in culture.
Project Dates:
July 1985–June 1988.

0614. VETERANS ADMINISTRATION MEDICAL CENTER, 700 19th Street, S., Birmingham, Alabama 35233.

Project Title:
The Use of Nicorette (Nicotine Resin Complex) in a Smoking Cessation Program.

Principal Investigator:
Bailey, W.C.
Objective:
To assess patient acceptance of Nicorette (nicotine chewing gum) as an adjunct to smoking cessation under field use situations.
Methods or Approach:
There are numerous reports in the literature of clinical studies using Nicorette, many involving double-blind, placebo, controlled designs utilizing rigidly monitored cessation programs. Results of such studies can be criticized as not strictly representing real-life situations. Also, duration of treatment with Nicorette was, in many studies, shorter than what is now considered optimal. It is therefore of interest to assess the usefulness of Nicorette as an adjunct to smoking cessation in a family physician environment. Nicorette has been made available to a broad spectrum of physicians to assess usefulness and patient acceptance in a limited number of patients who are serious about quitting. Patients are cigarette smokers who inhale smoke from at least one pack of cigarettes/day and are well motivated to stop smoking. Patients will be followed regularly in a clinic to evaluate cessation efforts and resolve any problems related to chewing Nicorette. Gradual withdrawal from the gum will be encourged at the 3-month visit. Patients who claim total abstinence for longer than 24 hours will have chemical verification by carboxyhemoglobin or expired air carbon monoxide measurements. The ultimate goal should be freedom from all forms of nicotine within 6 to 12 months.
Results to Date:
Results are not yet available.
Financial Support:
VA.

Arizona

0615. PULMONARY ASSOCIATES, P.A., 1130 East McDowell Road, Suite B-7, Phoenix, Arizona 85006.

Project Title:
Individualized Smoking Cessation Counseling Utilizing "Nicorette" Within the Setting of a Private Physician's Practice.

Principal Investigators:
Fahy, B.F.; Levine, B.E.
Objective:
To determine feasibility and efficacy of a smoking cessation program in a private physician's practice that utilized individualized counseling by a pulmonary clinical nurse specialist and use of "Nicorette" chewing gum.
Methods or Approach:
Smokers voluntarily enrolled in the smoking cessation program that consisted of six sessions over a 3-month period. At each visit, chewing gum and cigarette consumption was elicited by direct questioning. Counseling in the proper use of the nicotine gum, smoking diversion techniques, and personalized reinforcement were provided at each session by the nurse specialist.
Results to Date:
Of 42 persons choosing to enroll in the program (defined as attending more than one session), 21 had totally stopped smoking at the end of the program. Currently, 32 persons are enrolled, and followup data is not yet available.
Future Plans:
Patients who successfully completed the 3-month program will be contacted at 1 year to monitor status of smoking cessation.
Project Dates:
March 1984–March 1986.
Financial Support:
Pulmonary Associates.

0616. ST. JOSEPH'S HOSPITAL AND MEDICAL CENTER, BARROW NEUROLOGICAL INSTITUTE, 350 West Thomas Road, Phoenix, Arizona 85013.

Project Title:
Influences of Nicotine on Neuronal Expression of Acetylcholine Receptors.

Principal Investigator:
Lukas, R.J.
Objective:
To elucidate chronic and acute effects of nicotine on levels of expression and functional integrity of neuronal nicotinic acetylcholine receptors (nAChR).
Methods or Approach:
Simple experimental model systems will be developed for convergent study of nAChR structure and function. Clonal cell lines TE671 and PC12 will be maintained in continuous cell culture as models for central and autonomic neurons, respectively. The quantity of nAChR-like sites on the cells that interact with curaremimetic neurotoxins (nAChR-specific affinity reagent and cholinomimetic bromoacetylcholine) or with antibodies prepared against authentic nAChR from peripheral tissues will be assessed via standard ligand binding- or radioimmunoassays. Interrelatedness of sites that interact with different nAChR probes will also be explored by use of ligand competition binding assays. The quantity and disposition of sites on clonal cell lines and on fetal rat hippocampal and cerebral cortical cells in primary culture will be assessed via autoradiographic analysis of radiolabeled ligand binding patterns with respect to cellular morphological features. Levels of expression and integrity of functional nAChR will be ascertained by measurement of clonal cell uptake of isotopically labeled ions in response to application of nicotinic cholinergic agonist. When data have provided an adequate indication of the levels of putative and functional nAChR on cells in culture,

chronic and acute medium supplementation with nicotine (or in vivo administration to pregnant rats) will be employed and effects on expression of neuronal cholinoceptive elements will be ascertained.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–December 1987.
Financial Support:
CTR.

0617. UNIVERSITY OF ARIZONA, COLLEGE OF MEDICINE, Division of Respiratory Sciences, 1501 North Campbell Avenue, Tucson, Arizona 85724.

Project Title:
Pulmonary SCOR–Airways Obstructive Diseases.

Principal Investigators:
Burrows, B.; Lebowitz, M. D.
Objective:
To elucidate the pathogeneses, pathophysiology, natural histories, and factors contributing to the development of airway obstructive diseases (AOD) in order to prevent, detect, and/or treat AOD.
Methods or Approach:
A multidisciplinary program has been established involving and combining epidemiological, clinical, pathophysiological, experimental, and radiological approaches to the AOD problem. The prospective longitudinal epidemiological survey of 4,000 members of 1,650 Tucson households will continue to study the role of environmental, host, and genetic factors, including smoking, occupation, atopy, asthma, and history of bronchiolitis or other childhood respiratory illness, in contributing to the risk of developing asthma, chronic bronchitis, emphysema, or other AOD. Further opportunity is provided to evaluate methods for early detection of subclinical COPD. Annual questionnaires, pulmonary flow-volume curves, and chest radiographs will be evaluated in this context. In subpopulations there are specific studies of the role of aeroallergens, atopy and IgE levels, airway reactivity, elastase peptides or alpha-1-antitrypsin Pi MZ phenotype in development of AOD. Pediatric lung function tests are being developed and are being utilized in a separate subproject designed to study childhood airway diseases and their long-term consequences. Over 1,200 infants and their families have been enrolled in the project, which will also examine the effects of parental smoking on the respiratory status of the children.
Results to Date:
Characteristics of productive cough are somewhat different in a warm, dry climate, but relations to smoking still predominate and can be quantified. The smoking and pulmonary function relationship can be quantified. Smoking is also a critical factor in the relationship of a history of acute respiratory and childhood illnesses to obstructive airway diseases, and of occupational exposure and alcohol consumption to these diseases. Smoking and changes in smoking have now also been shown to be directly related to the presence of and the changes in obstructive airway diseases and associated syndromes. Passive smoking has not been found to be related to symptoms in family members. Smoking, IgE, and eosinophilia may react dependently and independently in relation to AOD. Atopy is related more to allergy and asthma, but smoking is related as well, especially to asthmatic bronchitis in older subjects.
Future Plans:
Appropriate immunologic, physiologic, pathologic, and radiologic studies will be done both in the population and in the laboratory to determine the pathogenesis of airway obstructive disease.
Project Dates:
June 1971–1986.
Financial Support:
NHLBI (HL-14136).

0618. UNIVERSITY OF ARIZONA, COLLEGE OF MEDICINE, Division of Respiratory Sciences, 1501 North Campbell Avenue, Tucson, Arizona 85724.

Project Title:
Environmental Factors in Obstructive Airway Diseases.

Principal Investigator:
Lebowitz, M.D.
Objective:
To study the effects of air pollution, aeroallergens, smoking, and meteorologic conditions on acute and chronic respiratory diseases.
Methods or Approach:
The total population under study is approximately 3,800 Anglo whites in a stratified cluster random sample of the Tucson community. The study of air pollution, aeroallergens, and meteorological effects on acute and chronic respiratory disease has been conducted in 117 families representing a disease-stratified random sample of the 1,600 families in the Tucson Epidemiological Study. They have been followed with daily diaries and peak flows for 2 years. Baseline immunologic and physiologic exams and respiratory history questionnaires have been completed, the latter including smoking histories. Smoking history is used in determining such effects as a control and as an interactive agent. Some pulmonary function measures included premecholyl and postmecholyl challenge studies. IgE studies will be conducted. Pollen, algae, fungi, and air pollutants have been monitored indoors and outdoors.
Results to Date:
Smoking is still the major factor in airways obstructive diseases. Passive smoking has not been found to be related to symptoms in adults, but may blunt children's responses to other irritants (as in experimental studies). Preliminary analyses of symptoms, peak flows of children, and environmental conditions note correlations with environmental conditions. Indoor and outdoor particulate, ozone, and pollen are related to symptom rates, more so in asthmatics.
Project Dates:
December 1976–1984.
Financial Support:
EPA (R805318); NHLBI (HL-14136); EPRI (RP 2378-5).

0619. UNIVERSITY OF ARIZONA, COLLEGE OF MEDICINE, Tucson, Arizona 85724.

Project Title:
Lung Structure and Function in Airways Obstructive Disease.

Principal Investigators:
Knudson, R.J.; Bloom, J.W.
Objective:
To elucidate pathophysiological mechanisms of airways obstructive disease; define changes in lung structure responsible for alterations in lung function.
Methods or Approach:
To examine subclinical effects of cigarette smoking, detailed studies of lung mechanics and pulmonary function were performed on 22 healthy middle-aged (40 to 60 years) current regular smokers and 19 controls, matched for sex and age, who had never smoked. None had a history of respiratory or heart

disease. Standard spirometry and measurement of single breath carbon monoxide diffusing capacity (D_L) were performed. Plethysmographic measurements included determination of lung volumes, air vs. helium-oxygen flow-volume curves, single breath nitrogen test, pulmonary resistance, and static deflation pressure-volume (P-V) curves using standard esophageal balloon techniques. The P-V curves were fitted to an exponential equation of the form $V = Ae^{-kP}$ where the constant k is an index of curve shape. Increased value for k reflects loss of lung elastic recoil.

Results to Date:

There were few abnormalities in lung function; only two smokers and one nonsmoker had forced expiratory volume in 1 sec (FEV_1) below normal range, and one smoker had a slightly low D_L and D_L per unit lung volume ($\%D_L/V_A$). However, there were systematic mean differences between smokers and nonsmokers. Compared with nonsmokers, smokers as a group had lower percent predicted FEV_1, lower FEV_1/forced vital capacity ratio, higher residual volume/total lung capacity ratio, lower D_L/V_A, and higher values for k. Even in this small group of smokers, the percent predicted FEV_1 showed a significant inverse correlation with pack-years of smoking. Of particular interest was the significant inverse correlation between $\%D_L/V_A$ and k. The shape constant k is markedly increased in emphysema and has been shown to correlate with size of airspaces. Although none of the smokers had markedly abnormal k values, it was postulated that the higher k values and lower D_L/V_A values may represent an accelerated aging effect with enlargement of terminal airspaces in smokers. It is concluded that even apparently healthy smokers exhibit some changes attributable to cigarette smoking.

Future Plans:

In longitudinal analysis of lung function data, similar detailed studies will be employed to physiologically characterize subjects who exhibit certain patterns of change over time that suggest development or clear evidence of chronic obstructive airways disease.

Project Dates:

December 1981–December 1986.

Financial Support:

NHLBI (HL 14136).

0620. UNIVERSITY OF ARIZONA, COLLEGE OF MEDICINE, Department of Physiology, 1501 North Campbell Avenue, Tucson, Arizona 85724.

Project Title:

Acute Cigarette Smoke Exposure Increases Alveolar Permeability in Rabbits.

Principal Investigators:

Witten, M.; Lemen, R.; Quan, S., et al.

Objective:

To (1) measure lung clearance of aerosolized technetium-labeled diethylenetriamine pentacetic acid (^{99m}TcDTPA) as an index of alveolar epithelial permeability in rabbits exposed to cigarette smoke; (2) establish a time course of cigarette smoke-induced increases of ^{99m}TcDTPA clearance in the rabbit; (3) ascertain whether changes were dose related; and (4) determine whether increases in ^{99m}TcDTPA clearance were associated with anatomical changes in alveolar or cellular structures.

Methods or Approach:

Eighteen rabbits were randomly assigned to (1) control (C); (2) all smoke exposure (ASE); or (3) limited smoke exposure (LSE). Cigarette or sham smoke was delivered by syringe in a series of 5, 10, 20, and 30 tidal volume breaths with a 20-minute counting period between each subset of breaths to determine ^{99m}TcDTPA biological half-life.

Results to Date:

Mean half-life minimum (smallest half-life) was significantly lower ($p<0.05$) for ASE and LSE rabbits compared with control values. A significant difference was observed at the 20- and 30-breath exposure levels between control and ASE group mean values (percent baseline) for half-life, arterial blood pressure, and peak airway pressure. Light and electron microscopy showed alveolar edema in ASE and LSE groups, but no alveolar-capillary membrane damage.

Future Plans:

The mechanisms responsible for increased ^{99m}TcDTPA alveolar clearance as a consequence of cigarette smoke exposure will be investigated.

Project Dates:

February 1984–1988.

Financial Support:

University of Arizona; NIH (BRSG2S07RROS675-16; NHLBI 07249; NHLBI 14136); Arizona Lung Association.

0621. VETERANS ADMINISTRATION MEDICAL CENTER, 3601 South Sixth Avenue, Tucson, Arizona 85723.

Project Title:

The Effects of Metoprolol and Propranolol on Airway Function of Persons With Minimal Airway Disease.

Principal Investigators:

Campbell, S.C.; Pinnas, J.

Objective:

To determine if cigarette smoking leads to decreased pulmonary function with metoprolol and propranolol; compare the pulmonary effects and pharmacokinetics of these drugs in smokers and nonsmokers.

Methods or Approach:

This is a latin-square, single-blind, single-dose within-patient pilot study. Ten smokers and ten nonsmokers will be studied. Subjects will be given placebo, propranolol (80 or 160 mg), and metoprolol (100 or 200 mg,) on separate days, and the following pulmonary functions will be measured: forced vital capacity, forced expiratory volume in 1 sec (FEV_1), forced expiratory flow at midpoint, maximum expiratory flow volume curves comparing air to a mixture of 80 percent helium and 20 percent oxygen, and airways resistance by body plethysmography. These tests will be measured at approximately 30 minute intervals for 2 hours and then at hourly intervals for 5 hours. Following this part of the study, each subject will be given 20 mg of metoprolol and propranolol intravenously on separate days. Blood levels of metoprolol and propranolol will be measured at frequent intervals during the first hour and at hourly intervals for the next 10 hours. Standard statistical analyses will be done to compare the pulmonary function test results on each medication of smokers with nonsmokers.

Results to Date:

No significant difference in the pulmonary function data of any of these tests was seen in smokers versus nonsmokers at any dose of medication versus placebo. The only statistically significant feature was that 160 mg of propranolol caused the FEV_1 to be lower at 5 hours compared with placebo or with the other medications in the smokers. Therefore, asymptomatic smokers are not at any increased risk to develop pulmonary problems while taking 160 mg propranolol or 200 mg metoprolol.

Financial Support:

VA.

0622. JOHN L. MCCLENNAN VETERANS ADMINISTRATION HOSPITAL, Veterans Administration Cooperative Study, Little Rock, Arkansas 72205.

Project Title:
The Effect of Smoking Cessation on the Natural History of Chronic Obstructive Lung Disease.

Principal Investigators:
McNabb, M.E.; Ebert, R.V.
Objective:
To determine whether smoking cessation alters the rate of decline in pulmonary function in patients with mild to moderate chronic obstructive lung disease, evaluate effectiveness of a special program designed to produce smoking cessation.
Methods or Approach:
Persons with mild to moderate chronic obstructive pulmonary disease will be followed with annual measurements of forced expiratory volume in 1 sec for 10 years. Subjects will be randomized into two groups for smoking cessation efforts: usual care and a group managed in a special clinic with psychological support and use of nicotine gum.
Results to Date:
Project is in a preliminary phase.
Financial Support:
VA.

0623. LITTLE ROCK VETERANS ADMINISTRATION MEDICAL CENTER, 4300 West Seventh Street, Little Rock, Arkansas 72205.

Project Title:
Studies on the Effect of Cigarette Smoking on Platelet Function.

Principal Investigator:
Mansouri, A.
Objective:
To determine if cigarette smoking or cigarette smoke (in vitro) can alter function of platelets.
Methods or Approach:
Platelets were obtained from smokers and nonsmokers and aggregation was determined. Platelets were exposed (in vitro) to smoke, carbon monoxide, or nicotine and aggregation and release reaction were studied. Platelet aggregation was determined by standard method using epinephrine, ADP, arachidonic acid, etc. The release reaction was performed using radioactive serotonin.
Results to Date:
Cigarette smoke through its carbon monoxide content inhibits platelet aggregation. Although this inhibition can be reproduced (in vitro) by inhalation of carbon monoxide, there is no good correlation between level of carboxyhemoglobin and impairment of platelet aggregation in heavy smokers. Carbon monoxide also significantly inhibits the platelet release function.
Future Plans:
To determine if prostaglandin metabolites are quantitatively different, platelets from smokers and nonsmokers will be examined.
Project Dates:
January 1981–January 1983.
Financial Support:
VA; AHA.

0624. UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES, 4301 West Markham, Little Rock, Arkansas 72205.

Project Title:
Particle Size Analysis of Cigarette Smoke Particulates.

Principal Investigators:
Hiller, F.C.; Anderson, P.J.
Objective:
To measure size distribution of cigarette smoke particulates.
Methods or Approach:
Test systems that utilize single particle aerodynamic relaxation time analyzer and electrical aerosol analyzer will be employed for measuring cigarette smoke size distribution.
Results to Date:
Results are being prepared for publication.
Future Plans:
The present work will be continued with studies of deposition of the particles in human subjects.
Project Dates:
July 1984–continuing.
Financial Support:
NIH; EPA (EPA HL20024, EPA R809098); ALA.

0625. UNIVERSITY OF ARKANSAS, Health Education Program, HP 308G, Fayetteville, Arkansas 72701.

Project Title:
Patterns of Smokeless Tobacco Use Among High School Students in Northwest Arkansas.

Principal Investigators:
Marty, P.; Young, M.; Williams, T., et al.
Objective:
To determine the prevalence of smokeless tobacco use in a high school population in northwest Arkansas; identify factors associated with behavior initiation and maintenance.
Methods or Approach:
A 26-item questionnaire was distributed to 901 students in two community senior high schools. Frequencies and cross-tabulations were employed to analyze data.
Results to Date:
Data indicate that 36.7 percent of male and 2.1 percent of female respondents use smokeless tobacco on a periodic basis. Among users, 46.9 percent have been users for 2 to 5 years; 15.4 percent report use for >5 years. Modal responses indicate that if smokeless tobacco is used at all, it is used on virtually a daily basis, and two to five dips/chews/day are most common. The factor most frequently cited as leading to use is the influence of a friend. Users report a multidimensional pleasure factor for continuing use. Alcohol is used concurrently by 70.7 percent of dippers/chewers, while smoking occurs in just over 25 percent of users. About 28.2 percent of users admit wanting to quit using smokeless tobacco. The belief is supported that a significant number of young people (mostly males) chew tobacco or dip snuff in this geographic area. Data suggest a need for developing interventions about smokeless tobacco that would assist young people in making informed decisions about the products.
Future Plans:
Further assessments will be made in various populations in Arkansas (rural vs. nonrural and white vs. nonwhite) related to smokeless tobacco use. Efforts to develop, implement, and

evaluate smokeless tobacco cessation programs are also planned.

Project Dates:
October 1982–continuing.

Financial Support:
University of Arkansas, Health Education Program.

0626. UNIVERSITY OF ARKANSAS, Department of Obstetrics and Gynecology, Division of Reproductive Pharmacology and Toxicology, 4301 West Markham, Little Rock, Arkansas 72205.

Project Title:
Effect of Personal Habits on Reproductive Function.

Principal Investigators:
Mattison, D.R.; Thomford, P.

Objective:
To define the effect of personal habits (e.g., recreational drug use, smoking, caffeine consumption) on reproductive function in women.

Methods or Approach:
Various research methods are used, depending on the reproductive endpoint being investigated.

Results to Date:
Studies in experimental animals have demonstrated that the ovary contains enzymes necessary to metabolize benzo(*a*)pyrene into products that destroy oocytes.

Future Plans:
The mechanism of action of ovarian toxins such as benzo(*a*)pyrene will be further characterized and the effects of cigarette smoke on hypothalamic-pituitary-ovarian function will be explored.

References:
(1) Shiromizu, K.; Mattison, D.R. "The Effect of Intraovarian Injection of Benzo(*a*)pyrene on Primordial Oocyte Number and Ovarian Aryl Hydrocarbon (Benzo(*a*)pyrene) Hydroxylase Activity." *Toxicology and Applied Pharmacology* 76:18-25, 1984. (2) Takizawa, K.; Yagi, H.; Jerina, D.M., et al. "Murine Strain Differences in Ovotoxicity Following Intraovarian Injection With Benzo(*a*)pyrene, (+)-(7R,8S)-Oxide, (−)-(7R,8R)-Dihydrodiol, or (+)-(7R,8S)-Diol-(9S,10R)-epoxide-2." *Cancer Research* 44:2571-2576, June 1984.

0627. UNIVERSITY OF ARKANSAS, 4301 West Markham, Little Rock, Arkansas 72205.

Project Title:
Endocrinologic Studies of the Gastrointestinal Tract (Mammals, Chickens).

Principal Investigators:
Rayford, P.L.; Chowdhury, P.

Objective:
To investigate the crossreactivity and interactivity of peptides in digestion processes.

Methods or Approach:
It is hypothesized that digestion processes are brought about by interactions between substances produced by the gastrointestinal (GI) tract, pancreas, and possibly the brain, and that the role of a single peptide is downplayed by these interactions. Research will investigate (1) chemical nature, biologic action, storage, and release of cholecystokinin (CCK)-like peptide found in brain and GI tract of several experimental animals, by radioimmunoassay and bioassay; (2) interrelationships between pancreatic endocrine and exocrine functions and release and actions of GI and pancreatic hormones; (3) release and interactions of GI and pancreatic hormones in animals in physiologic conditions over expanded periods of time; (4) interrelationships between release and biologic actions of GI and pancreatic hormones after neutralization of peptides with specific antibodies directed toward regions or toward all of the peptide molecule; (5) effect of cigarette smoke and of chemical agents that are found in cigarette smoke on release and actions of GI peptides and pancreatic endocrine and exocrine functions; (6) generation of specific antibodies by monoclonal antibody technique, to study actions of GI peptides and development of region-specific radioimmunoassays; (7) role of acute and chronic exogenous and endogenous CCK on satiety and subsequent weight loss in rats and dogs; and (8) interrelationships between hormones of GI, pancreatic, pituitary, and gonadal origin to determine if there is a centralized mechanism that controls release and actions of GI hormones. Radioligand-binding assays will be established to identify CCK and pancreatic polypeptide receptors in target tissues of peptides in several species of animals. Studies will be conducted to optiminze existing radioimmunoassays and to develop and validate newer systems for peptides that are currently not measured in the laboratory.

Results to Date:
Following intravenous cadmium (Cd) infusion in the presence of bombesin (peptide known to stimulate all GI hormones), Cd had little or no effect on release of gastrin, but exerted a latent effect on release of CCK and pancreatic polypeptide (PP). After intravenous infusion in presence of bombesin, nicotine showed an inhibitory effect of gastrin release and stimulatory effect on release of CCK and PP.

Project Dates:
February 1982–January 1987.

Financial Support:
NIADDK (5R01AM30215-03).

Reference:
Rayford, P.L.; Inoue, K.; Chowdhury, P. "The Influence of Cadmium ($CdCl_2$) on the Canine Plasma Levels of Gastrin, Cholecystokinin (CCK), and Pancreatic Polypeptide (PP)." *Biological Trace Element Research* 6:237-248, 1984.

0628. UNIVERSITY OF ARKANSAS, MEDICAL SCIENCES, Department of Physiology and Biophysics, 4310 West Markham, Little Rock, Arkansas 72205.

Project Title:
Mechanism of Action of Cadmium and Nicotine on GI Hormone Metabolism.

Principal Investigators:
Chowdhury, P.; Rayford, P.L.

Objective:
To (1) investigate the influence of cadmium and nicotine on basal and stimulated levels of gastrointestinal peptides; (2) determine effects on release, action, interactions, and storage of gastrointestinal peptides; and (3) determine if nicotine or cadmium influences weight gain.

Methods or Approach:
Sprague-Dawley or Long-Evans rats will be used and cadmium or nicotine at graded doses will be given either by oral intubation or via aerosol. Dose ranges selected will usually remain within levels expected in blood and tissues of average heavy smokers. Blood levels of nicotine or cadmium will be measured and correlated with gastrointestinal (GI) peptide levels measured by specific radioimmunoassay techniques. In addition, exposed animals will be evaluated for ability to stimulate exocrine pancreatic secretion under various stimulants such as secretin, bombesin, and cholecystokinin. Gastrointestinal peptides under acute and chronic states will also

be measured to assess effects on digestive processes. The mechanism of effect will be investigated using agonists and antagonists to GI peptide release.

Results to Date:
Data on distribution and retention of cadmium indicate that organs of the GI tract accumulate significant amounts of cadmium, significantly more than kidney or liver, which are the known major target organs. Studies in dogs (i.v. cadmium or nicotine) showed that neither cadmium nor nicotine affected basal levels of gastrin, cholecystokinin, and pancreatic polypeptide. However, under stimulation with bombesin, cadmium potentiated release of cholecystokinin and polypeptide; gastrin levels were not affected. Studies of cadmium on exocrine pancreatic secretions showed a stimulating effect on volume and protein and trypsin outputs. Pancreatic polypeptide release was potentiated by cadmium under secretin stimulations; further investigation using cholinergic antagonists indicated that PP release is mediated by cholinergic influences.

Future Plans:
Further studies will measure effect of acute and chronic exposure to cadmium and nicotine (oral or aerosol) on release of different GI peptides during basal states and after meals. Relationships between pancreatic bicarbonate, protein, trypsin, and volume and plasma levels of different GI peptides will be analyzed.

Project Dates:
February 1981–January 1986.

Financial Support:
NIH.

0629. VETERANS ADMINISTRATION 300 East Roosevelt Road, Little Rock, Arkansas 72206.

Project Title:
Effects of Use of Nicotine Inhalation and Nicorette Chewing Gum on Cigarette Consumption.

Principal Investigators:
McNabb, M.E.; Ebert, R.V.

Objective:
To (1) determine body exposure to nicotine from use of nicotine gum; (2) compare nicotine exposure from gum to that from cigarette smoking; and (3) assess acceptability and safety of sustained use of nicotine gum in persons with chronic lung disease.

Methods or Approach:
In 12 subjects, plasma nicotine levels were determined during hourly chewing of gum containing 2 mg nicotine and on another day during chewing of 4 mg gum. Nicotine levels from smoking were determined from 3 days of afternoon blood sampling. Twenty-five subjects were maintained on nicotine gum ad libitum for 6 months while determining plasma nicotine levels and observing side effects on multiple occasions. A gas chromatograph (GC) technique was used to measure plasma nicotine. Checklists were used for recording side effects.

Results to Date:
Chewing one piece of 4 mg nicotine gum hourly produced plasma nicotine levels that matched plasma levels from cigarette smoking. Use of 2 mg gum produces half these levels. Use of gum was very acceptable to patients. On average, self-dosage with nicotine gum led to nicotine levels that were lower than during smoking. Use of 2 mg nicotine gum never led to excessive levels of nicotine. When 12 or fewer pieces of 4 mg gum were used/day, excess levels were rare. Nicotine gum was safe.

Financial Support:
VA.

Reference:
Ebert, R.V.; McNabb, M.E.; McCusker, K.T., et al. "Amount of Nicotine and Carbon Monoxide Inhaled by Smokers of Low-Tar, Low-Nicotine Cigarettes." *Journal of the American Medical Association* 250(20):2840-2842, November 25, 1983.

0630. VETERANS ADMINISTRATION MEDICAL CENTER, 1200 West Third Street, Little Rock, Arkansas 72201.

Project Title:
Connective Tissue Metabolism Relating to Structural Defects in Man.

Principal Investigators:
Read, R.C.; Cannon, D.J.

Objective:
To examine the relationship of smoking and connective tissue damage.

Methods or Approach:
Sera and whole blood of patients presenting for repair of aortic aneurysm and Leriche syndrome will be examined for proteolytic and antiproteolytic activity. The role of copper in etiology of aneurysm formation will be examined in serum and hepatic samples. Serum elastolytic values were determined by radial diffusion on elastin-agarose plates; α_1-antitrypsin and α_2-macroglobulin levels by immunodiffusion assay; and α_1-antitrypsin phenotype by isoelectric focusing. Homogeneous populations of polymorphonuclear (PMN) leukocytes were isolated in modified Ficoll-Hypaque solution. PMN granules were then isolated by differentiated centrifugation and protein and elastolytic values determined. Tissue copper levels were determined by atomic absorption spectrophotometry.

Results to Date:
Significant differences in age, height, weight, and mortality were found between patients with Leriche's syndrome and those with abdominal aortic aneurysm. Smokers in both groups demonstrated marked leukocytosis. In smokers with aneurysm, serum and leukocyte elastolytic activity were significantly increased and serum antiproteolytic capacity reduced. Aneurysm patients have a higher incidence of inguinal herniation than Leriche's syndrome patients. Contrary to published reports, copper concentration in liver and skin is not reduced in aneurysm patients.

Financial Support:
VA.

References:
(1) Cannon, D.J.; Read, R.C. "Blood Elastolytic Activity in Patients With Aortic Aneurysm." *Annals of Thoracic Surgery* 34(1):10-15, July 1982. (2) Cannon, D.J.; Casteel, L.; Read, R.C. "Abdominal Aortic Aneurysm, Leriche's Syndrome, Inguinal Herniation, and Smoking." *Archives of Surgery* 119(4):387-389, April 1984.

0631. VETERANS ADMINISTRATION MEDICAL CENTER, 1200 West Third Street, Little Rock, Arkansas 72201.

Project Title:
Abdominal Aortic Aneurysm and Leriche's Syndrome in Smokers.

Principal Investigators:
Cannon, D.J.; Read, R.C.

Objective:
To examine effects of smoking on homeostasis of proteolytic-

antiproteolytic activity in patients with abdominal aortic aneurysm and Leriche's syndrome; describe role of copper metabolism and the copper enzyme lysyl oxidase in development of aortic aneurysms.

Methods or Approach:

A spectrum of biochemical assays will be performed on serum and leukocyte samples from control and documented patients to determine proteolytic, antiproteolytic, and oxidative changes. Copper levels and lysyl oxidase content of selected tissues will be analyzed. Many assays have been developed and others, such as lysyl oxidase activity, will be developed. Improvement of present assays by immunological detection (ELISA and RIA), including antigen purification and transmission and electron microscopic capabilities, will also be developed and used. Results should further reveal the nonpulmonary pathological damage of smoking and etiology of aneurysm formation.

Results to Date:

Results are not yet available.

Financial Support:

VA.

0632. VETERANS ADMINISTRATION MEDICAL CENTER, 300 East Roosevelt Road, Little Rock, Arkansas 72206.

Project Title:

A Study of Nicotine Tolerance in Smokers, Ex-smokers, and Nonsmokers Using Nicotine Chewing Gum.

Principal Investigator:

McNabb, M.E.

Objective:

To compare tolerance to body exposures of nicotine in nonsmokers, smokers, and ex-smokers.

Methods or Approach:

Demonstration of tolerance in smokers would support the concept of nicotine addiction in these people. Subjects will chew nicotine-yielding gum or placebo gum in a double-blind fashion. Symptoms of intolerance will be recorded and correlated with plasma levels of nicotine from samples drawn at occurrence of symptoms. Plasma nicotine will be measured by a gas chromatograph technique.

Results to Date:

Two nonsmokers and one ex-smoker demonstrated nausea and abdominal discomfort at plasma nicotine levels in the 5 to 10 ng/ml range.

Financial Support:

VA.

0633. VETERANS ADMINISTRATION, 300 East Roosevelt Road, Little Rock, Arkansas 72206.

Project Title:

The Influence of Breathing Gas of Increased Viscosity on Spirometric Expiratory Flow Rate Indices.

Principal Investigators:

McNabb, M.E.; Ebert, R.V.

Objective:

To see if expiratory flow rates measured by spirometry or pneumotachygraphy are retarded by inhalation of neon compared with air.

Methods or Approach:

Subjects in three categories (nonsmokers, smokers, and patients with chronic obstructive pulmonary disease) were asked to breathe a mixture of 74 percent neon, 5 percent sulfur hexafluoride, and 21 percent oxygen and then perform forced vital capacity maneuvers.

Results to Date:

Testing of subjects was completed. Small differences between air values and neon values occurred in both normals and abnormals with insufficient discrimination to suggest a useful test in the individual subject.

Financial Support:

VA.

California

0634. AMERICAN LUNG ASSOCIATION OF LOS ANGELES COUNTY, 5858 Wilshire Boulevard, Los Angeles, California 90036.

Project Title:

An Inter-Agency Smoking Cessation Program With Pregnant Women in the WIC Nutrition Centers.

Principal Investigators:

Simmons, R.A.; McCarthy, W.; Richwald, G.

Objective:

To pilot test a smoking cessation program with the Women, Infants and Children (WIC) Nutrition Centers in Los Angeles County; determine cost-effectiveness of offering the program to pregnant women.

Methods or Approach:

The program will include pregnant women who quit when they became pregnant to determine recidivism at 3 months after pregnancy termination. Through the Los Angeles Healthy Mothers–Healthy Babies Coalition, voluntary health agencies will develop a cessation education and counseling protocol and train WIC personnel in conducting monthly counseling sessions and regular education programs. Several WIC centers will participate and be pair-matched with random selection of experimental and control sites. Pregnant women will enter the program at time of entrance into WIC, and will be followed until 3 months after pregnancy termination. In addition to monthly counseling sessions, participants and designated significant others will receive regular phone calls from health agency volunteers providing encouragement and motivation. Besides traditional smoking and prognancy informational materials, participants will receive a photonovela sequel to a story about a pregnant woman and her family that follows her until 3 months after delivery. Materials will be developed by a local art college and will be geared specifically to the black population in southcentral Los Angeles participating in WIC. Women in experimental and control clinics will complete a pre- and postprogram interview on prenatal history, smoking history, sociodemographic information, social support, self-efficacy, and health locus of control. Saliva thiocyanate will be used as a marker to validate interview information.

Results to Date:

Project is in a preliminary phase.

Project Dates:

November 1984–December 1986.

0635. CITY OF HOPE NATIONAL MEDICAL CENTER, 1500 East Duarte Road, Duarte, California 91010.

Project Title:
Lung Cancer Screening of Workers at High Risk.

Principal Investigators:
Mittman, C.; Taylor, J.C.; Madison, R.

Objective:
To determine whether strategies can be developed to predict and/or prevent lung cancer in steel workers exposed to the coke oven environment.

Methods or Approach:
The project was facilitated by the Occupational Safety and Health Act and resulting Federal regulations that require some annual examinations for workers 45 years of age and older and/or with 5 years or more of employment. During the 5-year study, information was collected on job exposure, smoking history, family history of disease, and respiratory symptoms. Tests included lung spirometry and sputum cytology.

Results to Date:
It was found that spirometric measurements of forced expiratory volume in 1 sec (FEV_1) are significantly reduced in workers most exposed to coke oven emissions. Smoking and age were also significant predictors of abnormal FEV_1/forced vital capacity ratio. The most significant decrements in flow rate were seen in exposed workers and smokers with regular metaplasia and reactive bronchial epithelial cells.

Project Dates:
May 1979–August 1984.

Financial Support:
NIOSH (5RO1OH00914).

0636. CITY OF HOPE NATIONAL MEDICAL CENTER, 1500 East Duarte Road, Duarte, California 91010.

Project Title:
Heat Stable Alkaline Phosphatase (the Regan Enzyme): A Tumor Marker Reevaluated After Exclusion of Smokers.

Principal Investigators:
Muensch, H.; Maslow, W.C.; Azama, F.

Objective:
To determine the usefulness of heat-stable alkaline phosphatase as a tumor marker in patients with a negative smoking history.

Methods or Approach:
Significant elevations of heat-stable alkaline phosphatase (HSAP) have been found in a normal population of smokers. From 1,500 patients with a history of neoplastic disease, 286 patients with verified negative smoking history and clinically documented cancer were selected and blood samples were drawn. Levels of HSAP was compared with levels in a population of healthy smokers and nonsmokers. Using the substrate naphthol-ASNX-phosphate, a very sensitive fluorometric assay was developed that detects minute quantities of HSAP.

Results to Date:
HSAP was elevated above the normal range ($\geq$0.15 IU/L) in 24 percent of patients. At twice the upper limit level ($\geq$0.3 IU/L) 12 percent exceeded the limit. In 10 patients, HSAP showed higher elevation than CEA, and in 6 patients, HSAP was the superior marker (two lung, two pancreatic, and two ovarian cancers). In the samples from nonsmokers, 85 percent of abnormal results were found in 48 healthy smokers. Previous reports have failed to recognize the interference of smoking in use of HSAP as a tumor marker.

Financial Support:
City of Hope National Medical Center.

0637. CITY OF HOPE NATIONAL MEDICAL CENTER, 1500 East Duarte Road, Duarte, California 91010.

Project Title:
Heat Stable Alkaline Phosphatase: Serum Enzyme Levels in Smokers and Nonsmokers.

Principal Investigators:
Muensch, H.; Maslow, W.C.; Azama, F.

Objective:
To investigate activation by smoking of heat-stable alkaline phosphatase (HSAP), an enzyme normally produced in placental tissue, but also found in a variety of neoplasms.

Methods or Approach:
Serum levels of HSAP were measured in a population of apparently healthy smokers and nonsmokers.

Results to Date:
HSAP has been found in serum and tumor tissue of patients with a variety of neoplasms, and elevated levels of a placental-like alkaline phosphatase (PLAP-like AP) have been found in serum, saliva, and sputum of cigarette smokers. In 98 nonsmokers, mean serum level was 0.057 ±0.035 IU/L; in 65 smokers, mean level was 0.378±0.319 IU/L. Heat stability and immunological properties of PLAP-like AP appeared identical with the placental enzyme. In contrast, reactions with inhibitors such as L-phenylalanine, L-phenylalanylglycylglycine, L-leucine, and EDTA differed significantly. PLAP-like AP levels correlated with amount of smoking by a given individual; however, differences of more than tenfold were seen among smokers with comparable smoking habits. Cessation of smoking in eight subjects led to a decline in enzyme levels (half-life 6 to 9 days). Smokers with high PLAP-like AP levels were found to have higher CEA levels; also, smokers with high CEA levels were found to have higher PLAP-like AP levels.

Future Plans:
The source of enzyme production will be investigated; tissue localization will be demonstrated.

Project Dates:
January 1985–1986.

Financial Support:
City of Hope National Medical Center.

0638. COMMUNITY HEALTH PROJECTS, INC., 336 1/2 South Glendora Avenue, West Covina, California 91790.

Project Title:
Medical Attenuation and Withdrawal of Nicotine Dependence.

Principal Investigators:
Tennant, F.S., Jr.

Objective:
To identify and develop pharmacologic treatment agents that can attenuate and/or eliminate nicotine dependence.

Methods or Approach:
Various pharmacologic agents including mecamylamine, clonidine, and guanabenz acetate, are being used to facilitate medical withdrawal as adjuncts to nicotine gum.

Results to Date:
To date, mecamylamine appears to partially block nicotine dependence in humans. Other agents appear to have some attenuation of smoking behavior.

Project Dates:
July 1983–July 1985.

Financial Support:
Community Health Projects, Inc.

0639. DHHS, NATIONAL CANCER INSTITUTE, 746 Hawthorn Lane, Davis, California 95616.

Project Title:
Review and Evaluation of Smoking Cessation Methods: The United States and Canada, 1978-1983.

Principal Investigator:
Schwartz, J.L.

Objective:
To conduct a review and evaluation of smoking cessation methods in the United States and Canada.

Methods or Approach:
The project encompasses a review of methods in existence during the period from 1978 to 1983 and constitutes an update of the publication *Review and Evaluation of Smoking Control Measures: The United States and Canada, 1966-1977.* Relevant literature relating to smoking cessation methods will be identified and reviewed. Results of cessation methods will be analyzed and evaluated. The review will include unpublished work of investigators. Although it intends to focus on North America, the review will include European investigators for methods such as nicotine chewing gum and acupuncture. It will also include a listing of doctoral dissertations pertaining to cessation methods, produced between 1977 and 1983.

Results to Date:
Methods with maintenance components appear to improve quit rates. Behavioral methods (aversive procedures and self-management techniques) are the most frequent methods tested. Quit rates for current methods appear to be higher than for earlier methods.

Future Plans:
Results will be published in a National Cancer Institute monograph.

Project Dates:
September 1984–August 1985.

Financial Support:
NCI (N01CN35011).

References:
(1) Schwartz, J.L. "A Critical Review and Evaluation of Smoking Control Methods." *Public Health Reports* 84:483-506, June 1969. (2) Schwartz, J.L.; Rider, G. *Review and Evaluation of Smoking Control Methods: The United States and Canada, 1969-1977.* United States Department of Health, Education and Welfare, Public Health Service, Centers for Disease Control, Bureau of Health Education, DHEW Publication No. (CDC)79-8369, 1978.

0640. HARBOR-UCLA MEDICAL CENTER, 1000 West Carson Street, Torrance, California 90509.

Project Title:
Immediate Effects of Cigarette Smoking on Exercise.

Principal Investigators:
Hansen, J.E.; Hirsch, G.L.; Sue, D.Y., et al.

Objective:
To assess the immediate effects of moderate smoking on exercise capacity, including cardiovascular function, ventilation, and gas exchange.

Methods or Approach:
Nine healthy smokers (aged 19 to 35 years) were randomly assigned to two test days: smoking and nonsmoking. On the smoking day, sujects smoked three cigarettes/hour (85 mm long, nonfilter, 24 mg tar) for 5 hours. On the nonsmoking day, subjects received 3 hours of oxygen via nasal catheter to wash out carbon monoxide. On both days, spirometry, diffusing capacity, and specific conductance were measured at rest, followed by multiple measures of physiologic variables during incremental cycle ergometer exercise to tolerance. Statistical analysis was by analysis of variance, paired t-test, or sign test with $p < 0.05$ considered significant.

Results to Date:
Carboxyhemoglobin, rest and exercise heart rate, and dead space ventilation were higher on the smoking day; oxygen pulse, maximal oxygen uptake, and anaerobic threshold were lower. There were no significant changes in resting lung function or in rest and exercise blood gases. Findings indicate that cigarette smoking can cause immediately measurable adverse effects in healthy young adults (increased myocardial oxygen consumption and impaired oxygen transport and exercise capacity).

Project Dates:
January 1982–June 1984.

Financial Support:
PHS (NH-3078); NIH (GCRC RR 00425).

0641. KAISER FOUNDATION RESEARCH INSTITUTE, 3451 Piedmont Avenue, Oakland, California 94611.

Project Title:
Are Low-Yield Cigarettes Less Hazardous?

Principal Investigators:
Friedman, G.D.; Petitti, D.B.; Sidney, S.

Objective:
To investigate the health effects of smoking, with particular interest in cigarettes that have reduced yields of selected toxic constituents.

Methods or Approach:
Hypotheses are to be tested regarding significant differences between health effects of high-yield and low-yield cigarettes. A self-administered questionnaire is being completed by all Kaiser health plan subjects who are given a multiphasic health checkup (MHC) at the KFRI Oakland–San Francisco facilities since July 1979. It is expected that over 100,000 subjects will be involved. The questionnaire contains detailed questions on smoking habits, and more general questions on occupation, and on demographic/socioeconomic characteristics. Questionnaire responses, in conjunction with mortality and morbidity data (hospitalization, physician visits, days of incapacitation) and MHC data, are being analyzed for relationship between smoking habits and adverse health effects. The study is planned to last until 1989.

Results to Date:
It has been established that (1) questionnaires ascertain smoking habits at least as well as do physiological measurements; (2) prevalence of history of peptic ulcer among smokers is not related to tar/nicotine content of cigarettes smoked; and (3) passive smoking is highly prevalent among nonsmokers and its extent varies with age and other health-related characteristics.

Project Dates:
January 1979–continuing.

Financial Support:
NCI (R01-CA-36074).

0642. KAISER FOUNDATION RESEARCH INSTITUTE, Department of Preventive Medicine, 9985 Sierra Avenue, Fontana, California 92335.

Project Title:
Comparison of Two Methods of Risk Reduction Behavior Change.

Principal Investigator:
Ngo, E.
Objective:
To maintain and promote health of members of a health maintenance organization (HMO) by developing effective ways to reduce risk behavior associated with chronic diseases such as hypertension.
Methods or Approach:
Stress and smoking cessation interventions will be developed and tested, and two methods of delivery (self-directed and group instruction) will be compared. The sample consists of HMO members; one group a randomized selection from the total Fontana area membership of 250,000 and the other randomized from a list of persons who had attended the internal medicine or family practice clinics within the past 3 years.
Results to Date:
To date, 19 persons have signed up for smoking cessation workshops; 2 dropped out. There were 171 participants in stress reduction group sessions, with 12 dropouts. In the self-help category, 15 smokers received materials, and 142 persons requested materials on coping with stress. Results are not yet available.
Financial Support:
Kaiser Foundation Research Institute.

0643. KAISER-PERMANENTE MEDICAL CARE PROGRAM, Department of Medical Methods Research, 3451 Piedmont Avenue, Oakland, California 94611.

Project Title:
Methodologic Issues in Evaluating Stop Smoking Programs.

Principal Investigators:
Midanik, L.; Polen, M.R.; Hunkeler, E., et al.
Objective:
To assess three methodologic issues (definitions of smoking, period of followup, composition of study group) in 426 persons 5 years after participation in a stop smoking program of a prepaid medical plan.
Methods or Approach:
Data from participants in the Stop Smoking Clinic at the Oakland and San Francisco, California, medical centers of the Kaiser-Permanente Medical Care Program were collected on the 426 persons for 5 years after the program ended. Respondents were given a 15-minute telephone interview to assess smoking patterns over the 5-year period. Data were obtained by self-report for all periods throughout the study during which respondents reported that smoking occurred (smoking episodes).
Results to Date:
When smoking was defined by measurement interval or by type or amount of tobacco smoked, smoking rates varied only slightly. Little information was gained by extending followup beyond the first year. However, study group composition (as defined by attendance at program sessions) had a pronounced effect on smoking rates. Those who attended fewer sessions were more likely to smoke during followup.
Project Dates:
July 1983–December 1984.
Financial Support:
Kaiser-Permanente Medical Care Program.

0644. KAISER-PERMANENTE MEDICAL CENTER, 280 West MacArthur Boulevard, Oakland, California 94610.

Project Title:
Oakland Kaiser-Permanente Medical Center Stop Smoking Program: One Year Follow-Up.

Principal Investigators:
Taller, S.L.; Larson, P.J.; Pratt, J.W., et al.
Objective:
To determine success rate among the stop smoking program participants 1 year after completion of 13 group sessions; compare characteristics of quitters (those that did not smoke in the followup year) with those of smokers (those that smoked for any length of time in the followup year).
Methods or Approach:
Participant information is obtained through profile questionnaires before the sessions, rosters completed during the sessions, and followup telephone interviews a year after sessions are completed. Statistical data are developed to provide a profile of program participants; chi-square is applied to variables to compare quitters with smokers.
Results to Date:
At 1-year followup, 59 percent had remained abstinent and 58 percent of those who continued to smoke had reduced daily consumption. Compared with smokers, quitters attended more program sessions, increased sugar use, gained more weight, and were more satisfied with marriage or overall quality of life. Program participants were equally divided between men and women and between single and married. Mean age was 40 years. Participants smoked approximately 28 cigarettes/day for a mean of 21 years; 90 percent had tried to quit smoking at least once before.
Project Dates:
January 1982–November 1982.
Financial Support:
Kaiser-Permanente Medical Center, Oakland.

0645. LOMA LINDA UNIVERSITY, SCHOOL OF HEALTH, Loma Linda, California 92350.

Project Title:
Slide/Tape Programs on Effects of Smoking, Targeted Towards Adult Population.

Principal Investigators:
Hardinge, M.G.; Knopper, M.
Objective:
To get smokers to stop smoking.
Methods or Approach:
Library research will be conducted and behavior modification techniques will be studied to produce slide/tape presentations on the effects of smoking.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–October 1985.
Financial Support:
Loma Linda University.

0646. MAXICARE RESEARCH AND EDUCATION FOUNDATION, 11633 Hawthorne Boulevard, Hawthorne, California 90250.

Project Title:
Smoking Cessation in Pregnancy: A Self-Care Approach.

Principal Investigators:
Ershoff, D.; Danaher, B.; Mullen, P., et al.

Objective:
To (1) evaluate the effectiveness of the self-help program in getting women to stop smoking during pregnancy and/or to keep women who had recently stopped smoking from relapsing during pregnancy; (2) compare effectiveness with standard prenatal care that refers women to a group-based program and counseling from medical personnel; (3) determine whether behavioral differences between program participants and controls are of sufficient magnitude to translate into a reduced incidence of low birth weight deliveries and reduced utilization during the first 6 months of life; (4) determine whether the smoking behavior achieved by participants during the prenatal period is more likely to be sustained during the postnatal period than behavior of those in the control group; (5) establish whether the behavioral and health outcome effects of the self-help program are of sufficient magnitude to yield a favorable cost–benefit ratio; and (6) examine the between-group relationships of sociodemographic, pregnancy history, attitudinal, and situational variables that might differentially influence program effectiveness.

Methods or Approach:
The study population will be comprised of pregnant smokers entering prenatal care at a Los Angeles based health maintenance organization. During the 18-month recruitment period, approximately 600 will be randomly assigned by an obstetrical nurse to either the experimental or the control condition. All smokers will be enrolled regardless of level of motivation to stop smoking or degree of interest in smoking cessation programs. During an initial prenatal conference, women assigned to the home correspondence program will be introduced to the program by the nurse, who will briefly discuss the health risks of smoking and give the subject the first of eight program booklets. The other booklets will be mailed to the subject's home at weekly intervals. Women in the control group will receive factual information regarding smoking during pregnancy and will be encouraged to enroll in the smoking cessation program offered through the HMO health education department. Both groups will receive advice about smoking from the obstetrician and other medical personnel, who will not know the group assignment of any patient. No effort will be made to change the nature and amount of advice normally given by medical providers. A baseline screening questionnaire will be completed by all subjects during the initial prenatal conference. At approximately the seventh month of pregnancy, women will be interviewed by telephone about smoking status. An external validator (urine cotinine and nicotine sample) will be obtained at the fourth and seventh month.

Results to Date:
Project is in a preliminary phase.

Project Dates:
March 1985–June 1988.

Financial Support:
NCHSR (1R18HS05128-01); Maxicare Research and Education Foundation.

0647. PREVENTION RESEARCH CENTER, PACIFIC INSTITUTE FOR RESEARCH AND EVALUATION, 2532 Durant Avenue, Berkeley, California 94704.

Project Title:
The Napa Drug Abuse Prevention Project.

Principal Investigators:
Schaps, E.; Moskowitz, J.M.

Objective:
To conduct process and outcome evaluations of seven school-based substance abuse prevention programs that focus on improving school and peer group influences along with student attitudes and competencies.

Methods or Approach:
Twelve experimental or quasi-experimental evaluation studies were conducted over a 3-year period involving over 7,000 students. In each study, data were collected at pretest, posttest, and followup. School-related outcomes, such as self-esteem and academic achievement, were assessed in addition to drug-specific outcomes, including cigarette attitudes and use. Program implementation was assessed through student or teacher reports and classroom observations. A communitywide annual drug survey was conducted for grades 7 through 12 from 1979 to 1981.

Results to Date:
A drug education course for seventh grade students had some positive effects on drug knowledge and drug use (including cigarette smoking) and perceptions of peers' attitudes toward drugs and drug use. Students learned about their needs and motives, decisionmaking, commercial advertising techniques, assertiveness skills for dealing with peer pressure; practiced setting personal goals; and were provided information about tobacco, alcohol, and marijuana. The positive effects, however, occurred primarily for girls, and generally failed to replicate across the three drug education evaluations. None of the other programs that focused on risk factors associated with adolescent drug use (e.g., self esteem) but did not address the topic of drug use was found to be effective. Results have been published, and the document cites the 26 other project publications and research reports.

Project Dates:
August 1978–June 1983.

Financial Support:
NIDA (R18DA02147).

Reference:
National Institute on Drug Abuse. *The Napa Drug Abuse Prevention Project: Research Findings.* Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse, DHHS Publication No. (AOM) 84-1339, 1984.

0648. PREVENTION RESEARCH CENTER, PACIFIC INSTITUTE FOR RESEARCH AND EVALUATION, 2532 Durant Avenue, Berkeley, California 94704.

Project Title:
National High School Alcohol and Drug Policy Study.

Principal Investigator:
Moskowitz, J.M.

Objective:
To discover the extent to which students' use of alcohol, cigarettes, and drugs constitute problems for public high school administrators; determine the manner in which schools handle such problems.

Methods or Approach:
A national survey of high school administrators will be conducted by mail, utilizing a probability sample of 750 public high schools. The school's student discipline policy and procedures will be the focus of the investigation.
Results to Date:
Project is in a preliminary phase.
Project Dates:
April 1984–March 1986.
Financial Support:
NIAAA (AA06282-02).

0649. RANCHO LOS AMIGOS MEDICAL CENTER, PROFESSIONAL STAFF ASSOCIATION, 7413 Golondrinas Street, Downey, California 90242.

Project Title:
Acute Effects of Carbon Monoxide in Individuals With Coronary Artery Disease: A Multi-Center Study.

Principal Investigators:
Hackney, J.D.; Selvester, R.H.; Linn, W.S.
Objective:
To reevaluate the scientific data base concerning health effects associated with carbon monoxide and ambient or near ambient exposure levels in subjects with angina pectoris.
Methods or Approach:
Rancho Los Amigos Medical Center is one of three centers in the multicenter cooperative study. Subjects (approximately 24) will be middle-aged male patients recruited for cardiac rehabilitation programs, who have objectively documented coronary artery disease with consistent induced angina, and who are currently nonsmokers. Subjects will be exposed (on separate occasions) to clean air (control) and two different concentrations of CO relevant to ambient exposures. Exercise stress testing will take place outside the chamber before and after CO exposures. Blood samples will be collected and carboxyhemoglobin (COHb) levels determined by co-oximetry. Subject response will be measured in terms of time to develop angina during exercise and in ST segment changes on the electrocardiogram.
Results to Date:
Preliminary data has been collected on (1) accuracy and precision of COHb measurements; (2) generation of varying concentrations of CO and determination of gas stability over time; (3) pilot studies conducted to verify linearity and reproducibility of CO loading in human subjects; (4) determination of CO loading rate constant determined as the slope of a least squares regression line fit; and (5) exercise stress test in chamber CO exposure protocol. Subject recruitment is underway and CO exposure studies will begin shortly.
Project Dates:
May 1984–May 1985.
Financial Support:
Health Effects Institute, Cambridge, Massachusetts.

0650. SAN BERNARDINO COUNTY MEDICAL CENTER, 780 East Gilbert Street, San Bernardino, California 92415-0935.

Project Title:
Sex and Smoking Difference in Duodenal Ulcer Mortality.

Principal Investigators:
Kurata, J.H.; Elashoff, J.D.; Nogawa, A.N., et al.
Objective:
To analyze data from the National Center for Health Statistics and other sources to support the hypothesis that cigarette smoking causes duodenal ulcer disease.
Methods or Approach:
Mortality figures for duodenal ulcer are based on an enumeration of all death certificates in the United States from 1921 through 1980. Numbers of duodenal ulcer deaths and smokers were examined through time for males and females.
Results to Date:
The relationship between duodenal ulcer mortality and cigarette smoking was examined using Pearson correlation coefficients (r) and attributable risk (AR). There was a strong positive correlation between smoking and ulcer mortality over time for both sexes (males, $r = 0.76$; females, $r = 0.74$). AR, which measures the percentage of duodenal ulcer mortality directly attributable to smoking, ranged from 42 percent to 56 percent in males and from 36 to 43 percent for females.
Future Plans:
More detailed analyses of hospitalization and mortality data will be performed using cohort models.
Project Dates:
July 1983–continuing.
Financial Support:
NIAMDDK (AM 17328); Center for Ulcer Research and Education; Smith Kline and French Laboratories.

0651. SAN FRANCISCO GENERAL HOSPITAL, Chest Service 5K1, 1001 Potrero Avenue, San Francisco, California 94110.

Project Title:
Smoking Increases Respiratory Epithelial Permeability as Assessed by Aerosolized Solute Clearance.

Principal Investigators:
Huchon, G.J.; Murray, J.F.
Objective:
To investigate the influence of smoking on aerosol deposition and respiratory epithelial permeability.
Methods or Approach:
Four groups of subjects were studied: healthy nonsmokers, healthy smokers, patients with chronic obstructive pulmonary disease (COPD) who smoked, and COPD patients who did not smoke. All subjects were given a radioactive aerosol to inhale, and clearance of radioactive particles from the lungs was monitored by an external detector.
Results to Date:
Results show that whether or not COPD was present, respiratory epithelial permeability was increased in people who smoked.
Future Plans:
Studies will determine the exact site of aerosol deposition so that the membranes injured by smoking can be identified.
Project Dates:
December 1980–February 1983.
Financial Support:
NHLBI (HL19155); NATO (12482).

0652. SANTA CLARA VALLEY MEDICAL CENTER, 751 South Bascom Avenue, San Jose, California 95128. STANFORD UNIVERSITY MEDICAL SCHOOL, Stanford, California 94037.

Project Title:
Stress in Pregnancy Outcome in Teenagers.

Principal Investigators:
Hensleigh, P.A.; Barnett, C.; Moses, L.

Objective:
To test the following hypotheses: (1) psychosocial stress during pregnancy causes physiologic alterations that contribute to occurrence of fetal growth retardation, preeclampsia, preterm birth, and labor abnormalities; (2) stress, measured psychologically and biologically, is modifed by social support, self-confidence, mood, and coping; and (3) stress is positively related to adverse health behaviors during pregnancy and may augment known detrimental effects.

Methods or Approach:
The study will monitor social and psychological stress, physiological indicators of stress, and pregnancy outcomes experienced by women under the age of 18 years (group 1). Psychosocial stress will be serially measured using interviews and questionnaires. Biologic responses to chronic maternal stress will also be serially quantitated by urinary catecholamine and cortisol assays. To control for potentially stress-reducing effects of study interviews with group 1 subjects, a second group will consist of pregnant women below the age of 18 from whom only initial visit and postpartum data will be collected (group 2). The extent of patient knowledge and their behavior with regard to smoking, alcohol consumption, and drug use during pregnancy will be determined. Medical records will be used to document weight gain during pregnancy, onset and number of prenatal visits, and time lapse between onset of symptoms and treatment in those with preterm labor or premature rupture of membranes. Data will be analyzed to show the relationship between stress levels (measured psychologically and biologically) and potentially detrimental health behaviors. Dependent variables will be multiple assessments of fetal and neonatal condition. Evidence of compromised intrauterine fetal growth will be based on early ultrasound documentation of gestational age. Beginning in the 34th week, ultrasound measurements of fetal biparietal diameter, abdominal circumference, and estimation of amniotic fluid volume will be obtained every 3 weeks. Fetal compromise will be further determined by testing of fetal heart rate reactivity with nonstress tests at 37 weeks' gestation. At birth, medical or obstetric complications, neonatal size and development, and newborn illnesses or need for intensive care will be documented.

Results to Date:
Project is in a preliminary phase.

Project Dates:
December 1984–July 1985.

Financial Support:
Scripps Foundation.

0653. SRI INTERNATIONAL, 333 Ravenswood Avenue, Menlo Park, California 94304.

Project Title:
Effects of Oxidants on Production of Lung Lesions.

Principal Investigator:
Freeman, G.

Objective:
To study effects of long-range exposure to realistic concentrations of nitrogen dioxide (NO_2) and ozone (O_3) on health of monkeys; determine relative significance of NO_2 in the ambient atmosphere with that in tobacco smoke.

Methods or Approach:
Monkeys (*Macacus arctioides*) were exposed continuously to NO_2 in atmospheres containing either 2 or 9 ppm for about a decade. A few animals were exposed similarly for shorter periods to either 0.9 ppm O_3 or to a mixture of 0.9 ppm O_3 and 0.9 ppm NO_2.

Results to Date:
Prolonged exposures resulted in morphologic changes, mainly in the small airways, affecting epithelial and subepithelial tissue. Macrophages accumulated in all animals. The higher concentration of NO_2, resembling that in tobacco smoke, extended its effects to proliferation of the epithelium of proximal alveoli and was associated in some animals with distention and marked attenuation of peripheral alveoli. This led to enlarged total lung volumes and increased residual volumes with some destruction of alveolar tissue in one monkey with advanced disease (continuously exposed to high-dose NO_2). Accelerated erythrogenesis was a regular response to exposure and tended to subside with time. Generally, results were confirmatory of extensive previous experience with rats and compatible with available clinical epidemiology and morbid pathogenesis in smokers, including lack of evidence for induction of serious pulmonary disease in nonsmoking residents of smoggy atmospheres. Results are consistent, however, with reports of increases in minor respiratory disease, especially in children.

Project Dates:
1972–1983.

Financial Support:
EPA (68-02-1944).

0654. STANFORD CARDIAC REHABILITATION PROGRAM, 730 Welch Road, Stanford, California 94304.

Project Title:
Occupational Work Evaluation Soon After Heart Attack.

Principal Investigators:
Debusk, R.F.; Taylor, C.B.; Houston-Miller, N., et al.

Objective:
To (1) determine efficacy of intervention designed to facilitate early return to work following myocardial infarction; (2) investigate effects of audiotape smoking cessation program combined with phone calls by a nurse in uncomplicated post-myocardial infarction patients; and (3) determine if ongoing monitoring of self-efficacy to avoid relapse can be used to predict and avoid relapse.

Methods or Approach:
Two hundred previously employed men who sustained an uncomplicated myocardial infarction and are medically eligible to undergo early exercise testing will be randomized to intervention or usual care. At 3 weeks, intervention patients will undergo a symptom-limited treadmill exercise test followed by counseling by a physician and nurse, which will include information about test results, prognosis, and resumption of customary activities. Patients are provided with an at-home health enhancement program on videocassette, including materials on smoking cessation, stress management, and physical activity. Outcome measures include medical, psychological, occupational, and economic status at 6 months. Smoking outcome measures include serum thiocyanates and self-reported smoking rates.

Results to Date:
Eighty patients have completed intervention or usual care. Because of low baseline smoking rates, there are no differences between intervention and usual care patients at 6 months for percentage of individuals smoking, although intervention patients still smoking at 6 months report smoking fewer cigarettes than usual care patients who still smoke.

Project Dates:
July 1983–June 1986.

Financial Support:
NHLBI (HL 18907).

0655. STANFORD RESEARCH INSTITUTE (SRI INTERNATIONAL), Department of Behavioral Medicine, 333 Ravenswood Avenue, Menlo Park, California 94025.

Project Title:
Identification of Variables Associated With Maintenance of Nonsmoking in Ex-Smokers.

Principal Investigators:
Swan, G.E.; Rosenman, R.H.
Objective:
To identify predictors of long-term maintenance of smoking abstention in 160 males and 199 females who participated in formal smoking cessation programs and who have been abstinent for at least 3 months.
Methods or Approach:
Three assessment interviews were conducted over a 1-year period: intake, 6 months, and 12 months. At each interview, self-reported smoking status was corroborated with an assay for saliva thiocyanate. At intake, all subjects were assessed for general health, including pulmonary function, indices of stress such as type A behavior and daily hassles, smoking history, characteristics of the home and work environment, self-efficacy, withdrawal symptoms in the preceeding 3 months, and sociodemographics. At 6- and 12-month assessment, subjects were evaluated for pulmonary function, respiratory symptoms, hassles, weight, and details concerning either continued abstinence or return to smoking.
Results to Date:
Environmental and dietary habits were found to be significantly associated with saliva thiocyanate values. A method utilizing robust regression was proposed to reduce confounding effects to improve classification of abstainers and relapsers. Smoking cessation literature indicates that women generally do not do as well as men at long-term followup; therefore, analysis of NCSRS data was treated separately for males and females. Comparison of intake characteristics revealed that males tended to smoke more heavily and for longer periods of time, tended to report more physical withdrawal symptoms, consumed more caffeine and alcohol, and were more likely to be type A. Women were more frequently unemployed, more likely to report craving and depression as withdrawal symptoms, and reported higher total hassle severity. Univariate associations between intake characteristics and relapse during the 12-month period indicate that different predictors are present for male and female recidivists. Of the significant predictor variables, only self-efficacy and health habits are common to both groups of subjects.
Future Plans:
Analysis will continue with appropriate multivariate procedures. It is expected that future multivariate analysis will also model specifically the occurrence of relapse as a time-dependent process.
Project Dates:
October 1980–March 1985.
Financial Support:
NHLBI (N01HR12918).
Reference:
Swan, G.E.; Parker, S.D.; Chesney, M.A., et al. "Reducing the Confounding Effects of Environment and Diet on Saliva Thiocyanate Values in Ex-Smokers." *Addictive Behaviors* (In press).

0656. STANFORD UNIVERSITY MEDICAL SCHOOL, Stanford, California 94305.

Project Title:
Epidemiologic Methods–U.S. Uranium Miners.

Principal Investigator:
Whittemore, A.S.
Objective:
To reanalyze, using newly developed statistical techniques, the relationship between cigarette smoking and occupational radon daughter exposure to bronchial carcinoma among approximately 4,000 U.S. uranium miners.
Methods or Approach:
The study used probabilistic models of cellular carcinogenesis, combined with maximum likelihood statistical procedures for estimation of model parameters, to analyze lung cancer mortality among U.S. uranium miners. The parameters used in the models and estimated from the data would have biological interpretations, and would also be used to examine (1) the dose-response relationship for radon daughters exposure, particularly as it applies to low level exposures; (2) the nature and extent of interaction between radiation and smoking exposures in respiratory carcinogenesis; (3) the presence or absence of dose rate effect; (4) the effect of age at start of irradiation upon subsequent lung cancer risk; and (5) the evolution of risk after termination of exposure. To date, approximately 200 bronchial carcinomas have occurred in this cohort.
Results to Date:
A report of study findings has been prepared.
Project Dates:
September 1980–September 1982.
Financial Support:
NIOSH.

0657. STANFORD UNIVERSITY SCHOOL OF MEDICINE, Department of Gynecology and Obstetrics, Stanford, California 94305.

Project Title:
A Model of Adolescent Perinatal Risk Behavior.

Principal Investigator:
Hensleigh, P.A.
Objective:
To identify aspects of everyday life and personal experience that affect health behaviors during adolescent pregnancy.
Methods or Approach:
Behaviors of concern were those that are potentially modifiable, and a series of intensive interviews was conducted with 40 pregnant adolescents of Anglo and of Mexican descent (aged 17 years and under) in San Jose, California. Social context features identified that could affect health behavior and pregnancy outcomes included perceived stress, social support, school enrollment, self-care activities, future orientation, and parents' substance use. Variables were analyzed for effects on dependent variables (incidence and timing of use of cigarettes, marijuana, and alcohol, and use of prenatal services). Data for multivariate analysis were gathered in a close-ended survey of the population of child-bearing adolescents aged 17 or under who delivered in the San Jose area during a 6-week period in 1982.
Results to Date:
Multiple regression analysis showed that (1) use of different substances was not necessarily highly correlated (different factors account for the use of each substance); (2) there were no important differences between Anglos and Chicanos; (3) age

has a significant effect only on use of prenatal services, not on cigarette smoking; (4) social support has an affect on substance use (the more social support available the less likely the pregnant adolescent is to smoke cigarettes or marijuana); (5) adolescents with high levels of perceived stress are heavier cigarette smokers and cut down on marijuana smoking later in pregnancy than their peers; and (6) when parents' drinking and drug use and perceived stress are held constant, social support reduces incidence of cigarette and marijuana use.

Project Dates:
September 1981–January 1983.

Financial Support:
Health Services Administration (MCR-060466-01-0).

0658. STANFORD UNIVERSITY SCHOOL OF MEDICINE, Department of Pediatrics, Stanford, California 94305.

Project Title:
Transactions of Pregnant Adolescents in Prenatal Care.

Principal Investigators:
Litt, I.; Mendoza, F.; Heinrichs, W.L.

Objective:
To describe content of prenatal care; examine effect of content on health behavior during and subsequent to pregnancy, controlling for effects of patient and physician characteristics and setting in which care is delivered.

Methods or Approach:
Data are from a longitudinal survey of a convenience sample of 160 adolescents (aged 17 and under): all pregnant adolescent patients at four private physicians' offices, three county clinics, two private clinics, and a health maintenance organization. Audio tapes are made of two prenatal visits (second trimester and third trimester). Compliance with physician recommendations and the advice of social network members is assessed by home interview after the first taping, a phone call after the second taping, and followup calls at 2 weeks and at 2, 4, and 6 months after delivery. Information collected during the home interview includes measures of self-esteem, depression, anxiety, stress, and coping. Data on cigarette smoking are collected at all points except 2 weeks postpartum.

Results to Date:
Results are not yet available.

Future Plans:
The possibilities for developing a standard protocol for prenatal care and teaching materials on communication for physicians and nurse practitioners is being explored.

Project Dates:
February 1984–January 1986.

Financial Support:
Health Services Administration (MCJ-060495-02-0).

0659. STANFORD UNIVERSITY, STANFORD HEART DISEASE PREVENTION PROGRAM, Department of Medicine, Stanford, California 94305.

Project Title:
Nicotine Chewing Gum and Coping Skills Training in Smoking Cessation.

Principal Investigators:
Killen, J.D.; Maccoby, N.; Taylor, C.B.

Objective:
To investigate the effects of nicotine chewing gum alone and in combination with coping skills training in promoting abstinence following smoking cessation.

Methods or Approach:
The program is designed to evaluate a treatment which integrates psychological and pharmacological approaches to smoking relapse prevention. Adult smokers are assigned randomly to one of three conditions: (1) coping skills and nicotine chewing gum; (2) nicotine gum; and (3) coping skills. Self-efficacy scales designed to identify high-risk smoking situations are employed to enhance individualization of treatment. Withdrawal symptoms reports were collected daily during the first 2 weeks of treatment. Serum thiocyanate, carbon monoxide, and serum cotinine levels are analyzed at pre-, post- and followup periods to validate self-reports.

Results to Date:
Abstinence rates at 10.5 months following cessation were: (1) 50 percent for the group treated with nicotine gum and coping skills; (2) 30 percent for those treated with skills training only; and (3) 23 percent for those treated with nicotine gum only. Self-reports were validated by carbon monoxide determinations at 10.5 months.

Project Dates:
March 1982–November 1982.

Financial Support:
Dow Chemical Corporation.

Reference:
Killen, J.D.; Maccoby, N.; Taylor, C.B. "Nicotine Chewing Gum and Coping Skills Training in Smoking Cessation." *Behavior Therapy* 15:234-248, 1984.

0660. STANFORD UNIVERSITY, Health Research and Policy Building, Stanford, California 94305.

Project Title:
A Study of Self-Help Smoking Cessation and Maintenance.

Principal Investigator:
Fortmann, S.P.

Objective:
To (1) develop a self-administered maintenance program for nonsmoking; (2) assess the relative effectiveness of nicotine gum, placebo gum, or no gum in promoting long-term abstinence; (3) compare the relative efficacy of ad lib vs. continuous nicotine gum use regimens; (4) assess the effects of a psychological self-help maintenance program; (5) compare the relative effectiveness of different strategies for administering the psychological maintenance program; and (6) provide biochemical validation of subjects' smoking status for 2 years following cessation.

Methods or Approach:
Two factors will be included in the fully crossed experiment: (1) psychological factors, three levels (self-selected relapse prevention modules, randomly selected modules, and survey only); and (2) pharmacological factors, four levels (nicotine gum administered ad lib or on a continuous schedule, placebo gum, and no gum). The 1,200 persons who are able to quit for 48 hours will be randomly assigned to 1 of the 12 treatment cells. The relapse prevention modules will be mailed on a weekly basis for 8 weeks. Subjects will use self-efficacy scales to pinpoint "high-risk" situations and devise plans for coping with these situations. Assignments will be returned weekly. Nicotine and placebo gum will be given for 12 weeks. Mail-ins, financial deposits, and telephone prompts will be used to boost adherence to protocols. Assessment will be made of reported smoking, perceived self-efficacy, physical dependency, withdrawal symptoms, and side effects and carbon monoxide in expired air and saliva thiocyanate. Data will be collected at 0, 2, 6, 12, and 24 months.

Results to Date:
Project is in a preliminary phase.
Project Dates:
September 1984–August 1989.
Financial Support:
NCI (CA 38303).

0661. STANFORD UNIVERSITY, SCHOOL OF MEDICINE, Department of Family, Community and Preventive Medicine, HRP Building, Stanford, California 94305.

Project Title:
Reliability of Long-Term Dietary Recall.

Principal Investigator:
Whittemore, A.S.
Objective:
To assess long-term risk factor changes in communities exposed to varying levels of educational intervention to derive useful information about the long-term efficacy of chronic disease prevention programs involving behavior modification.
Methods or Approach:
A cohort of 800 men and women (aged 45 to 69) will be reinterviewed concerning dietary and alcohol intake in 1972, for comparison with results reported in 1972. Estimates of weight-for-height and of daily consumption of cholesterol, saturated and polyunsaturated fat, and alcohol will be computed and compared with corresponding estimates obtained from an identical questionnaire that was administered to the same subjects in 1972. Subjects will also be questioned about current dietary habits, alcohol consumption, smoking status, and physical exercise habits. Participants are residents of three northern California communities subjected to a coronary heart disease risk factor intervention study conducted in 1973-1975. A mass media health education campaign was carried out in two of the communities, with the third serving as a control. Using analysis of variance for each index, measures of intersubject variability at each time (1972 and 1983) and intrasubject variability between the two times will be examined. The measures will contribute useful information about the sensitivity and validity of personal interview techniques in case-control studies concerned with the role of diet, alcohol use, and smoking in cancer and in other chronic diseases that have long latent periods.
Results to Date:
Results indicate that among the 1,433 subjects from the Stanford Heart Disease Prevention Program Three Community Project in 1972, 1,040 could be traced with known address or telephone number in 1983. In this dietary recall study, 873 persons participated. There were 87 refusals, 40 persons were deceased, and 40 were unavailable for interview because of serious illness or language problems. Data have been checked and are ready for analysis. A statistical program for nutrient assessment, smoking index, and physical activity index is being developed.
Project Dates:
April 1983–April 1985.
Financial Support:
NCI (1RO1CA33940).

0662. STANFORD UNIVERSITY, STANFORD HEART DISEASE PREVENTION PROGRAM, Heart Research Program Building, Stanford, California 94305.

Project Title:
Self-Help Smoking Relapse Prevention.

Principal Investigators:
Killen, J.D.; Telch, M.J.; Fortmann, S.
Objective:
To examine effectiveness of self-help smoking relapse prevention treatments that combine nicotine or placebo chewing gum with self-administered relapse prevention materials.
Methods or Approach:
A 3 x 4 factorial experiment will be conducted with an expected 1,200 participants using two factors: chewing gum (nicotine/placebo) and self-help materials (self-selected/randomly selected). Subjects will be assigned to treatment conditions only after demonstrating ability to quit for 48 hours (low carbon monoxide reading). Subjects in self-selected groups will choose self-help materials based on rank ordering of their personal high risk situation. Subjects in the random condition will have no choice. Followup assessments will be made at 6, 12, and 24 months.
Results to Date:
Project is in a preliminary phase.
Project Dates:
September 1984–August 1989.
Financial Support:
NCI (1R01CA38303-01).

0663. STANFORD UNIVERSITY, STANFORD HEART DISEASE PREVENTION PROGRAM, Heart Research Program Building, Stanford, California 94305.

Project Title:
Effects of Nicotine Chewing Gum on Smoking Withdrawal Symptoms.

Principal Investigators:
Gottlieb, A.; Killen, J.D.; Taylor, C.B.
Objective:
To determine whether nicotine gum reduces withdrawal symptoms when expectancy and placebo effects are controlled for; whether nicotine gum reduces short-term relapse by reducing withdrawal symptoms.
Methods or Approach:
A 2 x 2 factorial design will be used (balanced placebo) with 100 participants; two groups will receive nicotine gum and two groups, placebo gum. With nicotine gum, one group will be told that they are receiving nicotine gum and the other group will be told that they are receiving placebo gum. In the placebo gum groups, one will be told that they are receiving nicotine gum and the other that they are using placebo gum. The major dependent variable will be withdrawal symptoms reported daily.
Results to Date:
Data are being analyzed.
Project Dates:
September 1984–October 1984.
Financial Support:
Merrell-Dow Pharmaceuticals Inc.

0664. STANFORD UNIVERSITY, STANFORD HEART DISEASE PREVENTION PROGRAM, Health Research and Policy Building, Stanford, California 94305.

Project Title:
Smoker's Challenge: Evaluation of a Community Smoking Cessation Contest.

Principal Investigators:
King, A.C.; Taylor, C.B.; Flora, J.A., et al.

Objective:
To evaluate effectiveness of communitywide contests designed to encourage individuals to quit smoking.
Methods or Approach:
Community-based approaches to smoking cessation may have the potential for reaching smokers who will not attend formal smoking cessation programs, and may also prove to be more cost effective. The first contest, concluded in the summer of 1984, involved two neighboring northern California communities. Participants, who had 6 weeks to stop smoking, were given information about available community and quit smoking materials. At the end of the 6-week period, a random drawing was held for the grand prize (trip to Hawaii) and 21 other prizes (donated). All winners verified nonsmoking status by submitting to alveolar carbon monoxide measurement and providing names of persons to contact. One month following the drawings, a questionnaire was sent to all entrants to assess current smoking status and habits. Three months post-contest, a random sample of 44 entrants who had quit (42 percent of those who reported having quit during the contest) were invited in for alveolar CO testing to determine smoking status. Also, a random sample (24 percent of entrants) of those who had not returned the post-contest questionnaire were contacted by phone to assess smoking status.
Results to Date:
The two validation strategies indicated a 16 percent quit rate at 3 months. Most entrants contacted by phone or questionnaire indicated that they had been able to quit during the contest, if only for several days. The 502 entrants were primarily chronic (mean years of smoking, 20), heavy (≥ 1 pack/day) smokers who had made few previous attempts to quit (79 percent reported 0 to 3 attempts). Almost all entrants reported that contest experience had encouraged them to try to quit again in the future. Findings are encouraging in light of the reduced cost and increased "reach" of this type of communitywide program. The 3-month quit rate was larger than that often achieved by minimal contact approaches. Additionally, the contest attracted entrants who were chronic smokers with a limited history of prior quit attempts, suggesting that this type of incentive approach is effective in motivating such smokers to move closer to quitting.
Future Plans:
The contest is currently being revised and expanded, for delivery in two targeted northern California communities in 1985. The contest will add interim prize drawings to assess their utility in enhancing participant motivation. All prizes will be procurred through donations. Cost–benefit analyses will compare contests with other types of smoking cessation programs.
Project Dates:
October 1983–September 1985.
Financial Support:
NHLBI (HL 21906).

0665. STATE DEPARTMENT OF HEALTH SERVICES, Resource for Cancer Epidemiology Section, 5850 Shellmound Avenue, Suite 200, Emeryville, California 94608.

Project Title:
Case Control Study of Respiratory Cancer and Employment History.

Principal Investigators:
Glazer, E.R.; Chiang, M.L.
Objective:
To investigate occupational/industrial risk factors for respiratory cancer.
Methods or Approach:
Telephone interviews were conducted with all cases who could be contacted, and with controls matched by sex, race, age (±5 years), and neighborhood or residence. Data on 346 case–control pairs were analyzed by multiple logistic risk analysis for matched pairs. Occupational/industrial risk factors investigated were duration of employment in blue-collar production occupations in five industrial categories: shipyard, petrochemical, metal-related, construction, and a heterogeneous "other" category. Other factors analyzed were asbestos exposure, cigarette smoking, vegetable consumption, dairy product consumption, alcohol intake, and education.
Results to Date:
With all factors in the analysis adjusted for each other, employment in blue-collar production occupations in shipyard, petrochemical, and construction industries was not associated with a statistically significant elevated risk. Thirty years of employment in the metal industry category and in the "other" category were associated with a moderately elevated risk. Examination indicated that the risk associated with the metal industry derived predominantly from the subset of laryngeal cancer cases. The case–control distribution of time spent in occupational categories suggests that respiratory cancer risks are associated with specific occupations rather than with broad industrial categories.
Future Plans:
Further analysis is planned to examine the associations of respiratory cancer and specific occupational categories with adjustment for smoking, and to explore additional cigarette smoking measures and dietary correlations.
Project Dates:
December 1978–1982.
Financial Support:
NIOSH (210-78-0070).

0666. UNIVERSITY OF CALIFORNIA AT LOS ANGELES, JONSSON COMPREHENSIVE CANCER CENTER, 10920 Wilshire Boulevard, Los Angeles, California 90024.

Project Title:
Unaided Smoking Cessation Project.

Principal Investigators:
Gritz, E.R.; Marcus, A.C.; Enstrom, J.E.
Objective:
To (1) design and carry out a prospective study of smokers who decide to quit without formalized external aid; (2) follow the sample for 6 months; (3) differentiate successful quitters from recidivists and nonquitters on dimensions of coping style and self-efficacy in response to high-risk situations; (4) develop recommendations based on the most successful techniques for achieving cessation and maintaining abstinence; and (5) develop a profile of former smokers in the adult U.S. population from preexisting data bases, using demographic, behavioral, and psychosocial information to differentiate successful quitters and recidivists.
Methods or Approach:
Smokers who intend to quit smoking on their own are recruited from several cohorts, including the Great American Smokeout and New Year's Day quitters. All subjects complete enrollment questionnaires, and a combination of mail-back questionnaires and telephone interviews are used to follow cessation efforts over a 6-month period. Subjects are divided

into two groups: (1) frequent contact, in which subjects complete questionnaires covering the first week of cessation, and telephone interviews at 1 week and at 1, 3, and 6 months; and (2) infrequent contact, involving telephone interviews at 1 month and 6 months after the first effort to stop smoking. All subjects are followed for 6 months (unsuccessful quitters, successful quitters, and recidivists). Nonsmoking prevalence and continuous cessation rates will be plotted over time. Primary methods of statistical analysis will be logistic regression and discriminate function analysis, to identify factors separating successful from unsuccessful quitters.

Results to Date:
Project is in a preliminary phase.

Project Dates:
January 1984–December 1985.

Financial Support:
ACS.

0667. UNIVERSITY OF CALIFORNIA AT LOS ANGELES, JONSSON COMPREHENSIVE CANCER CENTER, Division of Cancer Control, 10920 Wilshire Boulevard, Los Angeles, California 90024.

Project Title:
UCLA Smoking Cessation in Registered Nurses.

Principal Investigators:
Gritz, E.R.; Marcus, A.C.

Objective:
To (1) expand understanding of smoking among nurses; (2) measure effectiveness of a self-help smoking cessation program supplemented by a supportive environment among registered nurses in a hospital setting in lowering smoking rates; and (3) design an intervention that would be easily and economically available to nurses nationwide.

Methods or Approach:
The rate of smoking among nurses in the United states is higher than among any other group of health professionals, and smoking cessation among nurses has not kept pace with that of physicians, dentists, and pharmacists. Two hundred registered nurses and other hospital personnel who smoked were recruited at 15 Los Angeles area hospitals. Announcements for the self-help program were made through regular nursing service channels. Subjects filled out baseline questionnaires and were given the American Lung Association's smoking cessation self-help manuals supplemented by modules designed specifically for nurses. A 4-month blitz (posters, buttons, newsletters, stress management techniques) focused on encouraging smoking cessation in the nursing service environment. Program effectiveness is being evaluated with mailed questionnaires (1 month) and telephone interviews (6 months and 12 months). Self-reports of cessation are being objectively verified through confederate reports and by analysis of saliva for cotinine. A brief questionnaire is being administered to all nurses (2,000) at five hospitals in the program to assess current smoking status (prevalence) and efforts to stop smoking during the 1-year period prior to initiation of the program. Estimates of the spontaneous quit rate obtained will be compared with outcome data from the intervention program.

Results to Date:
Followup data are being collected.

Project Dates:
September 1983–August 1985.

Financial Support:
NCI (CCSP CA 36409-01).

0668. UNIVERSITY OF CALIFORNIA MEDICAL CENTER, Section of Endocrinology, 2025 Zonal Avenue, Unit 1, 18-632, Los Angeles, California 90033.

Project Title:
Interaction of Smoking and Prostaglandins.

Principal Investigators:
Nadler, J.L.; Horton, R.

Objective:
To (1) study the effects of nicotine-free, low-nicotine, and high-nicotine cigarette smoke on prostacyclin (PGI_2) and thromboxane (TXA_2) production in chronic smokers and nonsmokers; (2) investigate the direct role of nicotine and the adrenergic nervous sytem on prostaglandin alterations; and (3) evaluate the mechanism of tobacco smoke-induced vascular disease.

Methods or Approach:
Chronic smokers and nonsmokers will inhale smoke from a fixed number of nicotine free, low nicotine, and high nicotine cigarettes. Nicotine gum will be given to a group of abstaining chronic smokers and nonsmokers to evaluate the direct effect of nicotine. PGI_2 and TXA_2 changes will be evaluated by specific radioimmunoassay (RIA) of stable metabolites in urine; 6 keto $PGF_1\alpha$ and TXB_2, respectively. Platelet aggregation and TXB_2 in serum will also be studied. Further analysis of renal and extrarenal PGI_2 and TXA_2 production will be assessed using RIA and gas chromatography–mass spectrometry techniques. PGI_2 and TXA_2 changes will be correlated with plasma nicotine and cotinine levels. Various specific andrenergic agonists and antagonists will be administered during some studies to evaluate the role of the adrenergic nervous system activation in smoking-related prostaglandin changes.

Results to Date:
Chronic male smokers showed significant reduction of urinary PGI_2 (6 keto $PGF_1\alpha$) after smoking high-nicotine cigarettes or chewing nicotine gum; however, low-nicotine (<0.5 mg) and nicotine-free cigarettes did not alter 6 keto $PGF_1\alpha$ levels. Nonsmokers showed an increase in blood pressure after inhaling smoke from high-nicotine cigarettes or chewing nicotine gum, but showed no changes in 6 keto $PGF_1\alpha$. In contrast, inhalation of high-nicotine cigarettes or chewing nicotine gum increased the TXA_2 metabolite in urine of chronic smokers; α adrenergic activation produced by norepinephrine (NE) infusion produced significant increases in 6 keto $PGF_1\alpha$ in abstaining smokers and nonsmokers. However, the same dose of NE in chronic smokers during inhalation of high-nicotine tobacco prevented the rise in the PGI_2 metabolite. Results indicate that inhalation of smoke from high-nicotine tobacco in chronic smokers alters the normal balance of PGI_2 and TXA_2 in the vascular system.

Future Plans:
The effects of smoking and nicotine on PGI_2 and TXA_2 generation will be evaluated in chronic smokers with cardiovascular disease such as congestive heart failure, ischemic heart disease, and hypertension. Systemic and renal hemodynamics will be assessed. Other studies will include (1) the role of oral contraceptives and smoking on platelet function and PGI_2/TXA_2 balance and (2) the effect of smoking on lipoxygenase products of arachidonic acid, including 12 HETE from platelets and 15 HETE from blood vessels, which may have important roles in the pathogenesis of atherosclerosis in man.

Project Dates:
September 1983–September 1987.

Financial Support:
NIADDK (AM 07110); NHLBI (21112).

0669. UNIVERSITY OF CALIFORNIA, JONSSON COMPREHENSIVE CANCER CENTER, Division of Cancer Control, 1100 Glendon Avenue, Suite 844, Los Angeles, California 90024.

Project Title:
Psychology of Cigarette Advertising.

Principal Investigators:
Gritz, E.R.; McCarthy, W.J.
Objective:
To (1) examine the potential influence of cigarette advertising on adolescent perceptions of cigarette smokers and on their attitudes toward smoking in general; (2) show that adolescents can identify the desirable personality characteristics that advertisements of particular cigarette brands implicitly associate with smokers of that brand; and (3) provide evidence for an affirmative answer to the question "Can today's cigarette advertising influence adolescent nonsmokers to try smoking?"
Methods or Approach:
Approximately 1,000 children in the 6th, 9th, and 12th grades in Los Angeles area schools were given a 50-minute questionnaire to collect eight kinds of information; biographical data, cigarette smoking experience, major value orientation, major goal orientation, information about peer and significant-other smoking status, perceptions of personality characteristics of the smokers portrayed in selected cigarette ads, and preferences for selected cigarette ads and exploratory questions. Each student was asked to rate the perceived personalities of the models portrayed in three color prints of selected cigarette ads. A model in each advertisement was rated with 25 semantic differential scales. To enhance the validity of current smoking behavior, saliva samples were collected from all respondents, and saliva thiocyanate analysis was performed on a 10 percent sample. The two major hypotheses tested were that (1) students whose personality self-ratings were close to the personality ratings assigned to models portrayed in cigarette ads would be more likely to smoke, and (2) differences by grade in the ideal-self ratings would help to explain why younger adolescents are more vulnerable to perceived attractions of cigarette smoking.
Results to Date:
Multivariate analyses confirmed the first hypothesis for all males and 12th grade females but not for younger females. As predicted, difference scores decreased in absolute size with increasing favorableness towards future smoking for all males and for 12th grade females, but not for 6th or 9th grade females. Differences in patterns of ideal-self ratings between age groups were as expected. Where four factors could explain most of the common variance in ratings of 6th graders, six factors were needed to explain the common variance in 9th graders and seven for 12th graders. There was a tendency for a better fit of the predicted two-factor model for 6th graders and of the predicted three-factor model for 12th graders. Findings for teenagers' estimates of smoking prevalence were especially striking. Respondents grossly overestimated levels of smoking by adults and peers, yet tended to underestimate smoking by teachers.
Project Dates:
January 1982–1983.
Financial Support:
ALA.

0670. UNIVERSITY OF CALIFORNIA, INSTITUTE OF HUMAN DEVELOPMENT, Tolman Hall, Berkeley, California 94720.

Project Title:
Teenage Personality and Smoking: Longitudinal Studies.

Principal Investigators:
Clausen, J.A.; Livson, N.
Objective:
To (1) assess smoking behavior of longitudinal subjects now in their fifties and sixties; (2) relate smoking patterns or cessation of smoking to personality and social role involvement of study members as assessed in adolescence and periodically since then; (3) assess smoking patterns of adolescents and young adult offspring of study members; and (4) relate smoking patterns to personality assessed at an earlier period.
Methods or Approach:
Mail survey of study members and offspring regarding current smoking of cigarettes yielded a 91 percent return from study members, 85 percent return from offspring for whom adolescent personality assessments had been made 12 years previously, and 73 percent return from all other offspring over age 18.
Results to Date:
Findings are based on discriminant analysis, correlational analysis, and analysis of covariance. The most striking relate to sex differences in patterns of smoking cessation and personality correlates. Among smokers who had at maximum (usually at least 20 years ago) stayed below one pack of cigarettes/day, 77 percent of women stopped smoking compared with 62 percent of men; however, among those who had smoked at least one and one-half packs/day at maximum, only 27 percent of women smokers had quit compared with 63 percent of the men. Of men who had been heavy smokers, all but 6 percent said they had tried to stop, but nearly 25 percent of the women who had been heavy smokers said they had never tried to stop. Current smokers between 55 and 62 years of age differ little in personality from never smokers or those who had smoked, although smokers are slightly more likely to be seen as "pushing or stretching limits" and as undercontrolled ($p < 0.01$). Males classified by smoking histories in later middle life show few adolescent personality differences, but women who have not stopped smoking had difficult interpersonal relationships in adolescence that were reflected in their being seen as significantly more rebellious, undercontrolled, deceitful, lacking in personal meaning, self-indulgent, and unpredictable. Yet in the intervening years they have shed these negative attributes and are now seen as not significantly different from tobacco-abstinent peers. The answer to this pronounced personality change is currently being sought.
Future Plans:
Marital and work histories, using data only now becoming fully available, will be analyzed to determine whether (1) cigarette smoking serves a positive function for the women who cannot stop smoking; and (2) the inability to stop smoking is an indication of greater physiological dependence on the part of women who at some time become heavy smokers.
Financial Support:
NIDA (DA 2670); MacArthur Foundation.

0671. UNIVERSITY OF CALIFORNIA, SAN DIEGO SCHOOL OF MEDICINE, Medical Center, 225 Dickinson Street, San Diego, California 92103.

Project Title:
Uterine Blood Flow and Catecholamine Response to Repetitive Nicotine Exposure in the Pregnant Ewe.

Principal Investigator:
Resnik, R.
Objective:
To determine what nicotine dose administered to the pregnant ewe will produce plasma concentrations of nicotine similar to those found in human smokers; observe responses that occur in response to such concentrations.
Methods or Approach:
Late pregnant sheep are equipped with chronically implanted electromagnetic flow probes around both uterine arteries; catheters are placed in the arterial and venous sides of maternal circulation. In addition, fetal catheters were placed to measure nicotine concentrations in fetal circulation.
Results to Date:
A nicotine dose of 0.2 mg/min for 5 min resulted in mean plasma nicotine concentrations of 23.2 ± 1 ng/mL following infusion. This dose, administered for 5 minutes every 30 min over 4 hours produced no changes in catecholamines, uterine blood flow, or maternal and fetal physiologic characteristics. Since smoking is known to increase plasma catecholamines in humans, it is likely that the threshold for catecholamine release in sheep is greater than in humans, which should be considered when interpreting results in other species.
Project Dates:
January 1983–December 1984.
Financial Support:
CTR.

0672. UNIVERSITY OF CALIFORNIA, San Francisco, California 94143.

Project Title:
Pharmacokinetics and Pharmacodynamics - Developmental Considerations.

Principal Investigators:
Rudolph, A.M.; Benowitz, N.; Benet, L.Z.
Objective:
To examine pharmacokinetics of nicotine and its primary metabolite cotinine, in fetal and adult pregnant sheep.
Methods or Approach:
Pregnant sheep in the last trimester of gestation will have catheters inserted into a limb artery and vein and also into the uterine vein. Catheters will also be inserted and maintained chronically in fetal hind limb artery and vein, carotid artery, umbilical vein, and in the ammniotic and allantoic sac. After recovery from surgery, nicotine or cotinine will be given as a bolus or as a continuous infusion into the fetus or the pregnant sheep, and concentrations will be measured repeatedly to calculate clearance rates and distribution.
Results to Date:
Results are not yet available.
Project Dates:
August 1984–July 1987.
Financial Support:
NIGMS (GM 26691).

0673. UNIVERSITY OF CALIFORNIA, BERKELEY, SCHOOL OF EDUCATION, Berkeley, California 94720.

Project Title:
Substance Use and Abuse in Hyperactive Children.

Principal Investigator:
Lambert, N.M.
Objective:
To study substance use and/or abuse by children previously diagnosed and treated with stimulant drugs for a hyperkinetic disorder; determine whether the children use more drugs as medication and/or drugs of abuse during adolescence.
Methods or Approach:
Subjects include approximately 150 students identified as hyperactive, 50 behavioral equivalents who have a teacher rating on the Behavior and Temperament Survey equal to that of hyperactive children but no evidence of parental or physician concern about hyperactive behavior, and a random control group of 100 children. Self-reported substance use data constitute the major dependent variable. Parents and children are asked about use of beer, wine, cigarettes, hard liquor, marijuana, LSD, amphetamines and barbiturates (with and without prescription), cocaine, heroin, and glue. Behavioral characteristics and intellectual functioning are assessed by various rating scales. Subjects' home environment and family characteristics are evaluated through interviews conducted annually with children and parents.
Results to Date:
Pattern and progression of drug use were studied across a 1-year interval (T1, Spring 1981 to T2, Spring 1982) in 54 hyperactives and 47 controls aged 13 to 18. Findings showed that initiation rates for hyperactives did not differ significantly from controls; however, for cigarettes and nonprescribed barbiturates/tranquilizers, initiation rates for hyperactives were higher. Comparison of use rates during the 2 months prior to each report period (and in the past) also yielded few significant differences. However, hyperactives differed significantly from controls in reporting more frequent current use ($p<0.05$) and in a trend toward heavier lifetime use ($p<0.10$) of cigarettes at both T1 and T2. Patterns of drug involvement (using Guttman scalagram analysis) among hyperactives and controls differed relatively little between groups and in relation to conventional hierarchy of use established by Kandel; the first three steps were similar for both: (1) beer and wine, (2) hard liquor or cigarettes, and (3) marijuana. The next step in the sequence was pills for hyperactives; for controls it was cocaine. Data for progression of use suggests that hyperactives are less predictable than controls. Among nonusers at T1, more hyperactives than controls continued to be nonusers at T2, but two hyperactives compared with one control had initiated use of heroin by T2. Also, hyperactives progressed or regressed to drugs that were deviations from the pattern of involvement established with the Guttman scaling technique more often than controls.
Future Plans:
The potential influence of various familial and psychosocial factors in drug use between hyperactives and controls will be analyzed, including parental influences, peer influences, adolescent beliefs and values, types and lengths of drug treatment for hyperactivity, and evidence of associated learning disabilities.
Project Dates:
April 1981–March 1984.
Financial Support:
NIMH (5R01MH3563201-03).

0674. UNIVERSITY OF CALIFORNIA, BERKELEY, INSTITUTE OF HUMAN DEVELOPMENT, 1203 Tolman Hall, Berkeley, California 94720.

Project Title:
Smoking Motives: Bases for Prevention/Quitting Strategies.

Principal Investigator:
Livson, N.

Objective:
To investigate prospectively, for men and women within each of four smoker types, the predictability of age at starting to smoke cigarettes, maximum level of smoking, and ability to quit from adolescent personality dimensions available for original participants (born from 1920 to 1930) in three long-term longitudinal studies and for their offspring.
Methods or Approach:
Differences among smoking motives types (based on the Horn-Waingrow scale) and differences between each type and nonsmokers will be determined on adolescent personality measures (cluster-analytically derived dimensions, individual Q-sort items, and a composite measure of psychological health). Distinctions among smoker types in precocity, level, and quitting attempts/success will also be sought. Analyses will be carried out separately for men and women and for younger and older cohorts.
Results to Date:
Data indicate significant sex differences in smoking motives; women report smoking cigarettes more for pleasurable sensations and for reduction of negative affect than men.
Project Dates:
May 1984–April 1986.
Financial Support:
NIDA (1R01DA03514-01).

0675. UNIVERSITY OF CALIFORNIA, BERKELEY, Lawrence Hall of Science, Berkeley, California 94720.

Project Title:
Implementing Smoking Prevention and Cessation Education in California Schools.

Principal Investigators:
D'Onofrio, C.; Thier, H.D.
Objective:
To (1) provide, during each year of the 3-year project, 4,500 upper elementary and middle/junior high school students with an interactive, science-based smoking prevention and cessation program that will significantly contribute to reducing current smoking and preventing future smoking among participants; (2) develop necessary community leadership so that smoking prevention and cessation education becomes a regular ongoing part of the curriculum of participating schools and school systems; and (3) show a 10 percent reduction in smoking and a statistically significant shift in the positive direction in knowledge of health facts, beliefs about smoking, and intentionality to smoke in participating students.
Methods or Approach:
During each project year, five centers for dissemination of the Risk and Youth: Smoking Project, the American Cancer Society's Smoking Prevention and Cessation education program, will be established. The five center directors (university leaders in the sciences of health behavior) will each recruit 30 sixth, seventh, and eighth grade teachers to become involved in the project. The 150 teachers will be trained and monitored as they implement the program. Local American Cancer Society chapters will serve as regional resource centers for participating teachers and center director. Participating students will be evaluated for program impact.
Results to Date:
Project is in a preliminary phase.
Project Dates:
October 1984–October 1987.
Financial Support:
ACS.

0676. UNIVERSITY OF CALIFORNIA, BERKELEY, SCHOOL OF PUBLIC HEALTH, Department of Biomedical and Environmental Health Science, 101 Haviland Hall, Berkeley, California 94720.

Project Title:
CHD and Non-CHD Mortality in the Western Collaborative Group Study.

Principal Investigators:
Brand, R.J.; Rosenman, R.H.; Ragland, D.R.
Objective:
To (1) locate as many of the original participants of the Western Collaborative Group Study (WCGS) as possible during 1982 and 1983; (2) determine cause of death for those deceased; and (3) determine reasons for long-term mortality from coronary heart disease (CHD), cancer, and other causes.
Methods or Approach:
The WCGS is a large epidemiological study of CHD begun in 1960-1961 when 3,154 middle-aged men free of major diseases were assessed for a number of cardiovascular disease risk factors including cigarette smoking, serum cholesterol, and high blood pressure. Original participants are located using a variety of followup methods, and information relevant to cause of death for deceased is obtained from death certificates, clinical records, and pathology records. Information is coded for cause of death. Statistical analyses are conducted to test associations between risk factors noted at study entry and long-term mortality from various causes.
Results to Date:
Data from preliminary analyses indicate that high blood pressure, elevated serum cholesterol, and cigarette smoking are related to long-term CHD mortality. Type A behavior pattern had a strong association with early mortality, but the association is reduced for long-term mortality. Analyses for cancer and other non-CHD mortality have not been completed.
Future Plans:
In a planned followup, original participants will be given a physical examination and risk factors will be reassessed to determine reasons for incidence, as well as mortality, of several major diseases.
Project Dates:
June 1981–June 1986.
Financial Support:
NHLBI (HL26235); NCI (263-MD-014575-1).

0677. UNIVERSITY OF CALIFORNIA, DAVIS, TB 136, Occupational and Environmental Health Unit, Davis, California 95616.

Project Title:
Biological Monitoring of Human Sensitivity to Diesel Exhaust Exposure.

Principal Investigator:
Schenker, M.B.
Objective:
To (1) study determinants of mutagenicity in urine of railroad workers; (2) assess contributions to urinary mutagens from diesel exhaust exposure; and (3) assess determinants on urinary mutagenicity of cigarette smoking characteristics and passive cigarette smoke exposure.
Methods or Approach:
Urine samples, collected from approximately 150 railroad workers on 2 consecutive work days, were analyzed for mutagenicity by a modified liquid incubation assay. On the 2 sampling days, workers wore personal sampling pumps that were analyzed for diesel exhaust particles and for nicotine.

Workers also complete a questionnaire on active and passive cigarette smoke exposure and other potential causes of mutagenicity.
Results to Date:
Active cigarette smoking has a strong linear dose–response effect on urinary mutagenicity. Although cigarette tar content may contribute to urinary mutagenicity, more data are needed for evaluation.
Project Dates:
October 1983–July 1986.
Financial Support:
Health Effects Institute, Cambridge, Massachusetts.

0678. UNIVERSITY OF CALIFORNIA, IRVINE, Department of Community and Environmental Medicine, Irvine, California 92717.

Project Title:
Value of Selected Biomarkers in Developing a Risk Index of Asbestos-Related Disease in Shipyard Workers.

Principal Investigator:
Guirgis, H.A.
Objective:
To evaluate the utility of epidemiologic host factors and selected laboratory immunochemical markers in constructing an index which can be used for surveillance of malignant disease associated with environmental exposures, particularly asbestos in shipyard workers.
Methods or Approach:
This study will test the applicability of an index constructed from epidemiologic risk factors (e.g., smoking, environmental exposure, age, occupational history) and immunochemical markers (e.g., CEA, mitogen activation to PHA, percent T lymphocytes) in an experimental and a comparison group from the shipyard population. The value of the results will mainly be as a surveillance tool for workers exposed to asbestos to identify those at high risk (primary prevention), and/or to be used for early diagnosis of asbestos-related malignancies (secondary prevention).
Results to Date:
Results are not yet available.
Project Dates:
May 1980–1983.
Financial Support:
USN (NR 202-169).

0679. UNIVERSITY OF CALIFORNIA, IRVINE, MEDICAL CENTER, Department of Medicine, 101 City Drive, S., Orange, California 92668.

Project Title:
Airway Hysteresis in Chronic Obstructive Pulmonary Disease.

Principal Investigator:
Fairshter, R.D.
Objective:
To determine if airways of individuals with chronic obstructive pulmonary disease due to cigarette smoking exhibit hysteresis.
Methods or Approach:
Physiologic methods are used to characterize lung function, including expiratory flow rates, lung volumes, lung elastic recoil, and bronchodilator responsiveness. In addition, specific conductance and expiratory flow rates are determined at a specific lung volume before and subsequent to an inspiration to total lung capacity. Differences in specific conductance and flow rates on maneuvers preceding and following deep inspiration are considered an index of airways hysteresis.
Results to Date:
In normal subjects (controls), airway hysteresis was observed using expiratory flow and specific conductance studies. In chronic obstructive pulmonary disease, specific conductance and flow rates worsened after a deep breath, indicating that airways in such subjects not only fail to show hysteresis, but also that deep inspiration caused bronchoconstriction. Whether impairment of airway hysteresis is a risk factor predisposing to development of chronic obstructive lung disease or a result of airway damage caused by cigarette smoking is not clear.
Project Dates:
July 1981–June 1983.
Financial Support:
University of California, Irvine.
Reference:
Fairshter, R.D. "Airway Hysteresis in Normal Subjects and Individuals With Chronic Airflow Obstruction." *Journal of Applied Physiology: Respiratory Environmental Physiology* (In press).

0680. UNIVERSITY OF CALIFORNIA, LOS ANGELES, Department of Psychiatry, 760 Westwood Boulevard, Los Angeles, California 90024.

Project Title:
Hypnosis Treatment for Smoking.

Principal Investigator:
Holroyd, J.
Objective:
To determine the relationship of hypnotizability and certain motivational variables to long-term smoking abstinence after hypnosis treatment.
Methods or Approach:
Patients in a private psychological practice are seen for four hypnosis sessions. Standardized measures of hypnotic responsivity and motivation are obtained during the first session. Treatment is individualized, based on information gleaned from intake interview. After treatment, patients phone weekly and then monthly, to maintain contact. Six-month followup by the investigator will be related to the initial measures of motivation and hypnotizability.
Results to Date:
Results are not yet available.
Project Dates:
March 1981–1985.

0681. UNIVERSITY OF CALIFORNIA, LOS ANGELES, Non-Invasive Cardiology Laboratories, Los Angeles, California 90073.

Project Title:
Study of the Relative Cardiovascular Effects of Nicotine Taken in Two Forms.

Principal Investigators:
Jarvik, M.E.; Schneider, N.G.; Child, J., et al.
Objective:
To (1) compare the cardiovascular effects of nicotine in two forms and two doses–high- or low-nicotine-containing cigarettes and high and low doses of nicotine gum; (2) examine EKG and echocardiographic functions in smoking and determine whether nicotine gum acts similarly; and (3) establish the safety of using nicotine gum as a replacement therapy and weaning device during smoking cessation in normal smokers and in patients with heart disease or respiratory impairment.
Methods or Approach:
Subjects serve as their own controls in the testing of four

nicotine conditions: high-nicotine cigarettes (2.0 mg), low-nicotine cigarettes (0.2 mg), high-nicotine gum (4.0 mg), and low-nicotine gum (2.0 mg). A practice day allows familiarization with procedure. On test days, subjects arrive after morning abstinence and are given an electrocardiogram and an echocardiogram once before and at seven intervals after smoking a high- or low-nicotine-containing cigarette or before and after chewing a high- or low-nicotine-containing piece of gum (2 hours daily testing). In the first study, only healthy subjects will be studied. In the second study, patients with heart disease and/or respiratory impairment will be examined.

Results to Date:
Seven healthy subjects have completed testing. Data are currently being analyzed.

Project Dates:
February 1981–1983.

Financial Support:
Merrell-Dow Chemical.

0682. UNIVERSITY OF CALIFORNIA, LOS ANGELES, SCHOOLS OF MEDICINE AND PUBLIC HEALTH, 405 Hilgard Avenue, Los Angeles, California 90024.

Project Title:
Epidemiological Study of Chronic Obstructive Respiratory Disease in Los Angeles.

Principal Investigators:
Detels, R.; Rokaw, S.; Tashkin, D., et al.

Objective:
To (1) examine the relationship between air pollution and respiratory health among smokers and nonsmokers over 7 years in four areas of Los Angeles exposed to different levels and types of air pollutants; (2) do more extensive studies of the cross-sectional data collected on these four populations, and (3) look for changes in lung function over the course of 5 years in the four cohorts exposed to the different levels and types of pollutants.

Methods or Approach:
Residents of four geographically defined areas were invited to undergo spirometry, single-breath nitrogen test, and body plethysmography, and to respond to a standard respiratory questionnaire. Populations have been reexamined after a 5- to 6-year interval.

Results to Date:
Analysis of the cross-sectional study in the four geographic areas indicates that results of lung function tests are poorer for current smokers than for nonsmokers, and poorer for residents of areas subject to high levels of photochemical oxidants, pollutants, or SO_2 particulates and hydrocarbons. The magnitude of difference between study areas is greater for nonsmokers than for current smokers, but is evident in both groups. Analysis of changes in lung function test performance over a 5- to 6-year interval also showed greater declines in areas subject to high levels of both types of pollutants.

Project Dates:
October 1972–1985.

Financial Support:
EPA (R80620010); California State Air Resources Board (AO-133-32).

0683. UNIVERSITY OF CALIFORNIA, LOS ANGELES, Non-Invasive Cardiology Laboratories, 2025 Zonal Avenue, Los Angeles, California 90024.

Project Title:
Addict Smokers and Cessation With Nicotine Gum.

Principal Investigators:
Jarvik, M.E.; Schneider, N.G.

Objective:
To (1) identify "addict" smokers, i.e., those who experience withdrawal from nicotine per se; (2) define the nature, course, and duration of withdrawal symptoms and isolate those connected with primary reinforcement (nicotine) from those associated with habit cessation; and (3) determine experimentally the efficacy of nicotine gum in a replacement–extinction procedure where smokers are "weaned" off nicotine while they cold-turkey the secondary reinforcing components of the habit.

Methods or Approach:
In the current study, subjects are given physiological and psychological baseline tests before quitting and then are followed daily during cessation while on one of the two gums–placebo gum or nicotine gum. Clinic support is offered to each subject while undergoing testing and during all followup phases. In a second study, two groups will be added that will receive either placebo or nicotine gum but will not receive clinic support, to determine the role of such support systems in the comparisons of these two gums.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Questionnaires will continue to be tested (for predictive efficacy) and refined in a systematic way with the goal of producing a brief questionnaire that can distinguish among smoker "types." Specifically, one will be developed which will identify the smoker who is most likely to smoke for nicotine and continue to avoid withdrawal.

Project Dates:
January 1980–continuing.

Financial Support:
NIDA (R01 DA 02536-02).

0684. UNIVERSITY OF CALIFORNIA, LOS ANGELES, SCHOOL OF PUBLIC HEALTH, Los Angeles, California 90024.

Project Title:
Epidemiology of Cancer Among Mormons.

Principal Investigator:
Enstrom, J.E.

Objective:
To understand the reasons for the unusually low cancer death rate among active California Mormons as a whole; identify the subgroup of active Mormons with the lowest risk.

Methods or Approach:
Detailed demographic, lifestyle, dietary, occupational, and medical history data were collected in 1979 on 9,900 "active" California Mormon adults, specifically High Priests and their wives. Mortality followup will be conducted on this cohort for at least 6 years. Additional church-based mortality data will be collected for all California Mormons during the years 1980-1985 to increase the statistical reliability of the existing data summarized below. The data on lifestyle and health-related characteristics of "active" California Mormons will be related to detailed cancer mortality rates. Distinctive differences between these Mormons and other comparison groups will be highlighted. Major subgroups of active Mormon questionnaire

respondents will be defined with respect to low-risk cancer and total mortality.

Results to Date:

The standardized mortality ratio (SMR) for total cancer in 350,000 California Mormons during 1960-1979 and 750,000 Utah Mormons during 1970 and 1975, compared with U.S. whites, is about 50 percent for "active" males, about 65 percent for all males, and about 75 percent for all females. For active males the SMR is about 25 percent for smoking-related cancer sites and about 65 percent for all other sites. Mormons are a health-conscious religious group who appear to be similar to U.S. whites in many respects, such as diet, socioeconomic status, and urbanization, but who use substantially less tobacco, alcohol, coffee, and tea than the general population. "Active" Mormons, defined here to be church leaders known as High Priests, abstain almost entirely from tobacco, alcohol, and caffeine.

Project Dates:

1973–1986.

Financial Support:

NCI; ACS.

0685. UNIVERSITY OF CALIFORNIA, LOS ANGELES, SCHOOL OF PUBLIC HEALTH, Los Angeles, California 90024.

Project Title:

Smoking Cessation and Mortality Trends Among California Physicians.

Principal Investigator:

Enstrom, J.E.

Objective:

To determine how trends of cancer and total mortality, particularly lung cancer mortality, among California physicians since 1950 have been influenced by their high degree of smoking cessation.

Methods or Approach:

Using the 1950 American Medical Directory, a cohort of all 15,235 California male physicians has been established and followed for mortality through 1979. Followup is being continued through 1984.

Results to Date:

The standardized mortality ratio (SMR) for all causes for California physicians relative to U.S. white males declined from 84 percent during 1950-1959 to 67 percent during 1970-1979. The SMR for lung cancer declined from 62 percent during 1950-1959 to 30 percent during 1970-1979. The age-adjusted lung cancer death rate for California physicians has remained relatively constant, while rising among U.S. white males.

Future Plans:

SMRs and death rate trends for these and other smoking-related diseases have been published. The study is being expanded to include all 36,000 California physicians in 1970. Also, a health survey of a sample of current California physicians is being planned.

Project Dates:

1981–1986.

Financial Support:

NCI.

Reference:

Enstrom, J.E. "Smoking Cessation and Mortality Trends Among California Physicians." *British Medical Journal* 286:1101-1105, 1983.

0686. UNIVERSITY OF CALIFORNIA, LOS ANGELES, SCHOOL OF PUBLIC HEALTH, 405 Hilgard Avenue, Los Angeles, California 90024.

Project Title:

Epidemiology of Depression and Help-Seeking Behavior.

Principal Investigator:

Aneshensel, C.S.

Objective:

To provide estimates of the prevalence and incidence of depression and to identify causal factors and outcomes associated with this condition.

Methods or Approach:

Factors examined include life event stressors, physical health status, health care utilization, medication use, and social support networks. The study was conducted in two phases: (1) four interviews with a representative sample of Los Angeles County adults at 4-month intervals from 1979 to 1980; and (2) a fifth interview conducted with the same respondents in 1983 (4 years after the initial interview). Interviews were face to face for the first and fourth waves and by telephone at the remaining waves of data collection. At the time of the fourth interview (May 1980), a new community sample of 546 adults was randomly assigned to telephone or in-person interviews to assess the reactiveness of the panel study and the interview method effects. Owing to the large Hispanic community, interviews were conducted in English and Spanish.

Results to Date:

Smokers reported significantly higher levels of depression than nonsmokers as measured by the Center for Epidemiologic Studies–Depression (CES-D) index ($p < 0.05$). However, differences were not significant when analyzed by sex. There were no significant differences in the CES-D score when never smokers, ex-smokers, current smokers who wanted to quit, and current smokers who did not want to quit were compared. After controlling in a linear regression analysis for the effects of income, age, employment status, and sex, none of the smoking status variables contributed significantly to explaining the variance of the CES-D score. While both mental depression and smoking are major public health problems, results suggest that there is little relationship between the two in the general community.

Project Dates:

September 1978–continuing.

Financial Support:

NIMH (1MH32267-07).

0687. UNIVERSITY OF CALIFORNIA, LOS ANGELES, SCHOOL OF NURSING, Los Angeles, California 90024.

Project Title:

Environmental Metallic Ions and Immune Processes.

Principal Investigators:

Vredevoe, D.L.; Levy, L.

Objective:

To investigate effects of cadmium on immune responses of laboratory mice exposed to chronic doses of the metallic ion in drinking water; analyze mechanism of effects of cadmium on immune response by means of in vivo and in vitro assays.

Methods or Approach:

In in vivo studies, CBA/H male mice were given doses of cadmium chloride (30 to 300 ppm) in drinking water for periods of 6 weeks to 1 year. Clearance of sheep red blood cells, aggregated immunoglobulin G (IgG), and colloidal carbon was tested at various times during cadmium administration. In in vitro studies, two different populations of macrophages (thioglycollate elicited and control, nonelicited peritoneal macrophages) were compared to examine effects of cadmium on opsonin-dependent and opsonin-independent phagocytosis of radioactively labelled sheep red blood cells. A competitive internalization assay was done using unlabeled Fc fragments to study the internalization of ^{51}Cr sheep red blood cells coated with IgG.

Results to Date:

Phagocytic and immunological inhibition were observed to be reversible after chronic cadmium ingestion, shown in CBA/H mice given 30 to 300 ppm cadmium chloride in drinking water. Within 1 week after removal of cadmium drinking water, there was a return towards normal phagocytic and immunological function even in the presence of high cadmium concentration in tissues. The effect observed was greatest with opsonized sheep red blood cells, indicating a significant role of the Fc receptor. In vitro studies demonstrated that cadmium reversed this inhibition and caused an ingestion defect rather than a binding defect predominately on opsonized sheep red blood cells. Cadmium has been demonstrated to be present in cigarettes, cigars, and pipe tobacco and its presence in smoke from these sources may constitute a hazard for the smoker and nonsmoker.

Future Plans:

Analysis of the reversible effects of cadmium on immune responses will be conducted. The mechanism of this reversal may apply to other metallic ions.

Project Dates:

July 1981–June 1985.

Financial Support:

NIEHS (ES 02410).

0688. UNIVERSITY OF CALIFORNIA, LOS ANGELES, SCHOOL OF PUBLIC HEALTH, Center for the Health Sciences, Los Angeles, California 90024.

Project Title:

A Social Support-Enhanced Smoking Cessation Program for Blue Collar Workers.

Principal Investigators:

Brown, E.R.; McCarthy, W.J.; Gritz, E.R., et al.

Objective:

To assess the feasibility of adding a social support component to enhance effectiveness of an existing smoking cessation program.

Methods or Approach:

"FreshStart," the smoking cessation program used nationally by the American Cancer Society, is being compared with a program that resembles FreshStart in most respects, but that also includes training in skills needed to elicit social support from others and techniques for mobilizing social supportiveness of program participants for each other. A quasi-experimental design is being used in two worksite settings to evaluate effectiveness. The social support component being added (1) emphasizes the value of social support to persons trying to quit smoking; (2) provides instruction in techniques for voluntarily eliciting social support from friends, family, and coworkers; and (3) arranges for participants to select "buddies" (partners) in the smoking cessation group and instructs buddies to maintain daily telephone contact during the workshop period. Smoking status of all program participants, validated by carbon monoxide measures, will be determined at 3-month followup. The followup questionnaire will also collect information on quantity, quality, and type of perceived social support.

Results to Date:

Two medium-sized corporations in Los Angeles have agreed to encourage employees to participate and data are currently being collected.

Future Plans:

Findings will be used to design a more ambitious worksite-based smoking intervention for blue-collar workers.

Project Dates:

September 1984–August 1985.

Financial Support:

McArthur Foundation; ACS.

0689. UNIVERSITY OF CALIFORNIA, LOS ANGELES, 405 Hilgard Avenue, Los Angeles, California 90024.

Project Title:

Smoking Behavior and Pulmonary Risk Status.

Principal Investigators:

Tashkin, D.P.; Coulson, A.; Clark, V., et al.

Objective:

To (1) determine whether there are sets of characteristics that permit identification of cigarette smokers who are at particularly high risk of developing disabling chronic obstructive pulmonary disease; (2) ascertain whether there are facts that discriminate between individuals who quit smoking and those who do not; (3) evaluate influence of smoking cessation on respiratory symptoms and lung function; and (4) examine whether active smoking by one or more household members has an influence on respiratory symptoms and/or lung function of children and other household members who do not smoke (passive smoking).

Methods or Approach:

An intensive analysis of interrelationships of reported smoking behavior, lung function, and symptomatology, and other characteristics of some 15,000 persons participating in an ongoing prospective population study of chronic obstructive respiratory disease in four areas of Los Angeles County was conducted. As part of the analysis, changes in lung function, respiratory symptoms, and smoking behavior over a 5-year interval were examined.

Results to Date:

Data indicate that (1) teenagers who smoke start with higher than average lung function; (2) in 7- to 17-year-olds, lung function was reduced if at least the mother smoked; and (3) cessation of smoking in adults leads to early and sustained improvement in lung function of small airways, a trend toward improvement in forced expiratory volume in 1 sec, reduction in cough, and prevention of worsening of phlegm production and wheeze.

Project Dates:

April 1981–March 1983.

Financial Support:

NHLBI (R01HL2512-01A1).

0690. UNIVERSITY OF CALIFORNIA, LOS ANGELES, JONSSON COMPREHENSIVE CANCER CENTER, Division of Cancer Control, 10920 Wilshire Boulevard, Suite 1106, Los Angeles, California 90024.

Project Title:

American Cancer Society Surveys of Adult and Teenage Smoking. Phase I.

Principal Investigators:

Marcus, A.C.; Breslow, L.; Gritz, E.R.

Objective:

To (1) provide reliable and valid trend estimates of smoking prevalence and associated attitudes, beliefs, and behaviors in adolescents and adults; (2) identify target populations for statewide and local efforts at smoking prevention and cessation; (3) assess success of interventions at state and local levels; and (4) provide insight into dynamics of smoking behavior, including identification of particular attitudes, beliefs, support systems, and other factors that differentiate smokers from nonsmokers and successful quitters from unsuccessful quitters.

Methods or Approach:
Two statewide random-digit dialed telephone surveys are being designed: (1) adults aged 17 and older, and (2) adolescents aged 12 through 18. For the adult survey, interviewing will be on a continuous basis, with 2,000 interviews conducted yearly beginning in 1985. For the adolescent survey, interviewing will be on an episodic basis, with 3,000 interviews conducted every other year beginning in 1986. Questionnaire content will include current smoking behavior; initiation, maintenance, and cessation of smoking; attitudes and beliefs related to smoking; social variables; health care data; and demographics.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Data collection is expected to continue through the end of the century.

Project Dates:
October 1984–continuing.

Financial Support:
ACS.

0691. UNIVERSITY OF CALIFORNIA, LOS ANGELES, SCHOOL OF PUBLIC HEALTH, Center for the Health Sciences, Los Angeles, California 90024.

Project Title:
Social Support Modalities for Permanent Smoking Cessation.

Principal Investigators:
Fielding, J.E.; Ford, J.; McCarthy, W.J.

Objective:
To conduct a 2-year test of three different intervention modalities for getting people to quit smoking permanently.

Methods or Approach:
All three modalities included cognitive-behavioral strategies commonly employed in smoking cessation programs. Over 200 smokers who wanted to quit, recruited from corporate headquarters of two large California high technology firms, were randomly assigned to (1) cognitive-behavioral modality; (2) social support modality; or (3) lifestyle change modality. Two counselors conducted smoking cessation workshops and followup meetings. Workshops were held over 8 days (5 days the first week and 3 days the following week). All participants submitted a 25 dollar deposit at the beginning of the program, 10 dollars of which was to be refunded at the final workshop session, the rest at 12-month followup. Followup meetings were biweekly the first month and less frequent in successive months. The first modality focused exclusively on cognitive-behavioral methods; the second on strategies for eliciting social support thought necessary to maintain abstinence; and the third on the need to anchor a person's ex-smoker status by adopting other lifestyle changes, particularly exercise and nutritional habits. Evaluation will be made at 3-, 6-, and 12-month followup.

Results to Date:
About 80 percent of workshop participants successfully quit smoking by the eighth session; unfortunately, only about 25 percent of quitters had remained abstinent at 3-month followup. Final evaluations have not yet been completed. There appeared to be no significant difference between modalities. The only major predictors of abstinence were (1) willingness to attend followup meetings and (2) number of previous attempts at quitting. The more times people had tried to quit smoking in the past, the more successful they were in remaining abstinent for 3 months. Many participants who had returned to smoking considered themselves to have "dropped out" of the program and failed to attend scheduled followup meetings despite efforts to encourage them to quit again and to remain active participants in the cessation program.

Future Plans:
On the basis of final results (6- and 12-month evaluations), logistical and motivational issues involved in conducting a worksite smoking cessation program will be identified and used to propose a model of worksite smoking cessation that should be readily implementable in worksite settings in a variety of institutions and ought to be maximally effective.

Project Dates:
July 1983–June 1985.

Financial Support:
NHLBI (HL 30308).

0692. UNIVERSITY OF CALIFORNIA, LOS ANGELES, HARBOR-UCLA MEDICAL CENTER, 1000 W. Carson Street, Torrance, California 90509.

Project Title:
Prevention of Preterm Labor.

Principal Investigators:
Hobel, C.J.; Bragonier, R.J.

Objective:
To test the effectiveness of a prenatal care program of education and five specific interventions that may prevent women from delivering preterm infants.

Methods or Approach:
A randomized trial was conducted to test the effectiveness of the following interventions: (1) social service; (2) bed rest; (3) Provera tablets (IND-FDA approved); (4) placebo tablets; and (5) control. All groups receive an intense educational program that includes smoking reduction.

Results to Date:
Preliminary results (1.5 years) indicate that the experimental group has a reduced incidence of prematurity.

Project Dates:
September 1983–June 1986.

Financial Support:
California Maternal Child Health (84-84231).

0693. UNIVERSITY OF CALIFORNIA, LOS ANGELES, VETERANS ADMINISTRATION MEDICAL CENTER, Brentwood Division, Mail Code 691/B151D, Los Angeles, California 90073.

Project Title:
Chemosensory Reinforcement in Smoking Behavior.

Principal Investigators:
Jarvik, M.E.; Rose, J.E.; Herskovic, J.E.

Objective:
To identify some of the more important secondary reinforcers of cigarette smoking (e.g., taste, chemosensation, tar); characterize salience in smoking maintenance and satisfaction.

Methods or Approach:
The project concentrated on the taste and chemosensory stimuli produced by cigarette smoke as it passes through the lips to the alveoli of the lungs. This will be studied by selectively stimulating and blocking various portions of the

respiratory tract, using various aerosols and anesthetics (mainly lidocaine). Also under study is the peripheral receptor responsible for the bitter taste of nicotine on the tongue, with and without the nicotinic blocking agent hexamethonium. The role of tar in smoking satisfaction is being investigated using a smoke mixer that allows subjects to control the tar delivery of each puff.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Different isomers of nicotine will be used to see if the hexamethonium blockade of the bitter taste of nicotine on the tongue is stereospecific.

Project Dates:
January 1985–December 1986.

Financial Support:
ACS.

0694. UNIVERSITY OF CALIFORNIA, LOS ANGELES, VETERANS ADMINISTRATION MEDICAL CENTER, Brentwood Division, 691/B151D, Los Angeles, California 90073.

Project Title:
Determinants of Nicotine Seeking Behavior: Stress and Nicotine Levels.

Principal Investigators:
Jarvik, M.E.; Herskovic, J.E.; Rose, J.E., et al.

Objective:
To study the psychophysiological and psychological correlates of nicotine-seeking behavior under stressful and nonstressful conditions.

Methods or Approach:
By using a new smoke-mixing device, nicotine-seeking behavior can be measured under different conditions of stress to determine if people smoke more under stress because they specifically want more nicotine. Stress will be manipulated by using various cognitive and noncognitive tasks. To dissociate the peripheral sympathomimetic from the central calming effects of nicotine, the beta-blocker propranolol will be given before stressful tasks. It is hypothesized that propanolol will block peripheral cardiovascular effects of stress and that of nicotine, without disrupting the psychological calming effects of nicotine sought by smokers.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Nicotine levels will be manipulated to determine effects on psychophysiological and subjective measures of stress, with and without propanolol and other pharmacological blocking agents.

Project Dates:
January 1985–January 1987.

Financial Support:
John D. and Catherine T. MacArthur Foundation.

0695. UNIVERSITY OF CALIFORNIA, LOS ANGELES, Department of Psychology, 1282 Franz Hall, Los Angeles, California 90024.

Project Title:
Content Analysis of Mass Circulation Magazine Cigarette Ads During the Period From September 1980 to June 1983.

Principal Investigator:
McCarthy, W.J.

Objective:
To relate teenagers' cigarette brand choices, reported in surveys in 1981, 1982, and 1983, to cigarette advertisements appearing in mass circulation magazines appearing in the same period.

Methods or Approach:
All cigarette ads appearing in *Time, Newsweek, U.S. News and World Report, Ms. Magazine, Rolling Stone, People, Psychology Today, Sports Illustrated, Cosmopolitan,* and *TV Guide* between September 1980 and June 1983 are being analyzed for content. Categories include (1) age appropriateness of portrayed activity in theme ads, (2) amount of space devoted to tobacco product relative to nontobacco product themes, (3) nature of prosmoking theme, and (4) cigarette brand advertised. Results will be correlated with concurrent survey data of choices made by adolescents.

Results to Date:
Over 2,000 cigarette ads have been evaluated to date. "Tombstone" ads (which picture only a pack of cigarettes) are very unpopular with adolescent smokers. "Theme" ads, particularly those that devote >50 percent of ad space to a pictorial theme, are disproportionately attractive. Marlboro cigarettes, which averaged 87 percent of space devoted to pictorial themes (the highest of any brand), were the most popular brand among adolescent smokers (55 percent of adolescent smokers in Los Angeles). Other brands that had a high percentage of pictorial space and were popular with adolescents were Kool, Benson and Hedges, Winston, and Salem. Unpopular cigarettes were Cambridge, Now, Carlton, and Merit, which had health-related themes and tended to use the tombstone ad format. Tentative correlation between percent of ad space in theme ads devoted to pictorial theme and adolescent popularity of the brand is over 0.60.

Future Plans:
Results of data analysis will be used to justify prospective study of the influence of cigarette advertising on children's attitudes and behaviors with respect to cigarette smoking.

Project Dates:
September 1982–December 1984.

Financial Support:
University of California, Los Angeles.

0696. UNIVERSITY OF CALIFORNIA, LOS ANGELES, Department of Psychology, 1282 Franz Hall, Los Angeles, California 90024.

Project Title:
Social Communication Functions of Adolescent Smoking.

Principal Investigators:
McCarthy, W.J.; Feshbach, S.; Jarvik, M.E.

Objective:
To determine whether adolescents are attracted to cigarette smoking because it is perceived as a readily available means of increasing interpersonal skills.

Methods or Approach:
It was expected that adolescents who had a high need for affiliation, a low need for academic achievement, and a high need for independence of adult authority would be measurably more likely to smoke cigarettes than most adolescents. Cross-sectional survey data was collected on 2,498 7th through 12th graders in 1980-1981, 1,638 8th and 11th graders in 1982, and 1,163 9th and 12th graders in 1983. Questionnaires requested information on biographical data such as age, height, and family size (but not religion or ethnicity). Items related to smoking included age of first smoking, number of cigarettes smoked last week, and cigarette brand smoked. Scales included

measures of need for affiliation; ability to establish solid relations; social dominance; smoking-influenced social dominance; smoking-influenced ability to establish solid relations with others; and beliefs about the addictiveness of cigarettes, aesthetics of smoking, stimulation value of smoking, and physiological reward of smoking. Social desirability was also measured. In the third year, questions about health-related behaviors (exercise and wearing seatbelts) were asked.

Results to Date:
Results do not confirm the hypothesis that adolescents initially smoke cigarettes to enhance communication skills, but do confirm the role that value of independence of adult authority and value of academic achievement play in predicting smoking behavior. Overall prevalence of smoking was 21.2 percent for males and 23.0 percent for females. More than half of all regular smokers smoked Marlboro cigarettes. Data confirmed that nonsmokers attribute greater social benefits to smoking than do smokers. Social skills that were predictive of smoking were ability to establish solid relations with others and social dominance. In all 3 years, subjects without older siblings were less likely to be smokers. Third-year data show that smoking was associated with more hours of parttime work, less exercise, and a greater belief in the role of luck than self-care in determining future personal health.

Project Dates:
July 1980–August 1984.

Financial Support:
NICHHD (HD 14402).

0697. UNIVERSITY OF CALIFORNIA, LOS ANGELES, CENTER FOR HEALTH SCIENCES, Department of Psychiatry and Biobehavioral Sciences, Westwood, California 90024.

Project Title:
Comparison of General and Subspecialty Internists in Counseling About Smoking.

Principal Investigators:
Wells, K.B.; Lewis, C.E.; Schleiter, M.

Objective:
To determine extent of counseling about smoking and exercise by general and subspecialty internists; compare extent of counseling between groups.

Methods or Approach:
A national sample of recent graduates of training programs in internal medicine will be surveyed; questionnaires will be administered to physicians and patients; physicians will complete encounter forms.

Results to Date:
Results are not yet available.

Project Dates:
June 1982–June 1985.

Financial Support:
Robert Wood Johnson Foundation.

0698. UNIVERSITY OF CALIFORNIA, SAN DIEGO, SCHOOL OF MEDICINE, Department of Community and Family Medicine, M-007, La Jolla, California 92093.

Project Title:
Rancho Bernardo Heart and Chronic Disease Survey.

Principal Investigators:
Barrett-Connor, E.; Wingard, D.

Objective:
To conduct a population-based prospective study of predictors of heart and chronic disease with a particular focus on diabetes mellitus.

Methods or Approach:
Followup has been conducted on 5,000 adults first studied in 1972-1974 to record morbidity and mortality. Baseline data included cigarette smoking, blood pressure, height, weight, cholesterol, and fasting plasma glucose. Cigarette smoking patterns in an upper class population and the effect of sex differences on outcome were determined.

Results to Date:
Cigarette smoking is a risk factor for coronary heart disease (after age 50) and for stroke. Passive smoking by nonsmoking women married to smokers increases the risk for coronary heart disease.

Project Dates:
June 1971–June 1988.

Financial Support:
NHLBI (N01-HV-12160-L); NIA (AM31801).

0699. UNIVERSITY OF CALIFORNIA, SAN DIEGO, SCHOOL OF MEDICNE, Department of Community and Family Medicine, M-007, La Jolla, California 92093.

Project Title:
Analysis of Peripheral Arterial Disease Data.

Principal Investigator:
Criqui, M.H.

Objective:
To (1) investigate etiology of large vessel peripheral arterial disease and small vessel peripheral arterial disease by evaluating the association of certain cardiovascular disease risk factors with peripheral arterial disease (PAD); (2) evaluate degree of association between PAD and subsequent cardiovascular disease (CVD) morbidity and mortality on a population basis to determine whether noninvasive tests of PAD can be utilized as a predictor of CVD; and (3) correlate conjunctival microvasculature pathology with CVD risk factors and noninvasively assessed small vessel PAD and large vessel PAD.

Methods or Approach:
The study group consists of patients selected for hyperlipidemia (50 percent) and a random sample of a defined community (50 percent). Information was collected on multiple risk variables, including diet, medications, alcohol use, cigarette smoking, past medical and surgical history, history of vasectomy, height and weight, blood pressure, arcus senilis, cholesterol, triglycerides, high density lipoprotein, low density lipoprotein, and very low density lipoprotein cholesterol, cholesterol/triglyceride ratio in very low density lipoproteins, apoprotein E and its subfractions, fasting plasma glucose, glycosylated hemoglobin, and immunoglobulin E. The dependent variable, PAD, was measured by four noninvasive tests: segmental blood pressure, flow velocity by Doppler ultrasound, postocclusive reactive hyperemia, and pulse reappearance time. For the second objective, and PAD-CVD association, PAD measurements will be used as the independent variable and CVD morbidity and mortality will become the dependent variable. The third objective will be addressed by a comparison of computer analysis of image-enhanced photographic negatives of the conjunctival microvasculature with CVD risk factors and test results on small and large vessel PAD.

Results to Date:
Results are not yet available.

Project Dates:
July 1978–June 1984.

Financial Support:
NHLBI (5R01HL22255-04).

0700. UNIVERSITY OF CALIFORNIA, SAN DIEGO, SCHOOL OF MEDICINE, Department of Community and Family Medicine, M-007, La Jolla, California 92093.

Project Title:
Support of Analysis of LRC Program Clinical and Epidemiological Data Sets.

Principal Investigator:
Criqui, M.H.
Objective:
To evaluate whether cigarette smoking and alcohol consumption have any effect on cardiovascular morbidity and mortality through a pathway involving two lipoproteins (high density lipoprotein cholesterol and low density lipoprotein cholesterol).
Methods or Approach:
Two separate Lipid Research Clinic data sets (followup study and coronary primary prevention trial) are being used. In both studies, alcohol and cigarette smoking will be evaluated for relationship with cardiovascular morbidity and mortality. Statistical analysis will be used to determine if smoking and alcohol have a major portion of their effect through a lipoprotein pathway (by affecting high density lipoprotein and low density lipoprotein).
Results to Date:
Preliminary data analyses have been completed.
Project Dates:
July 1984–June 1987.
Financial Support:
NHLBI (N01HV1260-L).

0701. UNIVERSITY OF CALIFORNIA, SAN DIEGO, SCHOOL OF MEDICINE, Department of Community and Family Medicine, M-007, La Jolla, California 92093.

Project Title:
Effects of Passive Smoking on Ischemic Heart Disease Mortality of Nonsmokers: A Prospective Study.

Principal Investigators:
Garland, C.; Barrett-Connor, E.; Suarez, L., et al.
Objective:
To determine whether exposure to smoke from a spouse who smokes increases risk of ischemic heart disease in a cohort of 695 nonsmoking women in Rancho Bernardo, California.
Methods or Approach:
The nonsmoking women (aged 50 to 79 years at entry), who have been closely followed, were divided into (1) married to nonsmoker; (2) married to ex-smoker; and (3) married to current smoker. There were 203 women in group 1, 395 in group 2, and 97 in group 3. Mortality and morbidity was recorded between 1972-1974 (entry dates) and 1983, and vital status was ascertained for 99.6 percent. Concurrent data are available of systolic blood pressure, plasma cholesterol, obesity index, and length of marriage to current spouse. Data are being used as covariates in a Cox regression approach to life-table analysis of outcome.
Results to Date:
Results have been submitted for publication.
Future Plans:
It is anticipated that the analysis will be repeated as the cohort ages, perhaps in about 3 years.
Project Dates:
1972–continuing.
Financial Support:
University of California, San Diego, School of Medicine; NIADDKD (RCDA 5K04AM01083-02); NHLBI (RCDA 5K04HL00946-03, HV1 2160-L).

0702. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, SCHOOL OF DENTISTRY, San Francisco, California 94143.

Project Title:
Smoking and Oral Cancer.

Principal Investigators:
Silverman, S., Jr.; Greenspan, D.
Objective:
To compare the following variables in patients with head and neck cancers (lips, oral cavity, nasopharynx, hypopharynx, larynx): (1) smoking habits; (2) tumor site and stage; (3) smoking habit after treatment; (4) status of tumor (control); (5) posttreatment tumors (other primary tumors); and (6) follow-up time.
Methods or Approach:
Patients with oral leukoplakia (n=257) were studied and followed for an average of 7.2 years; 73 percent used tobacco, mainly cigarettes.
Results to Date:
Forty-five patients subsequently developed squamous carcinomas; eight developed in patients who originally had epithelial dysplasia. High risks for malignant transformation included nonsmoking subjects, but in tobacco users, there appeared to be a decreased risk for malignant transformation when smoking was discontinued. An increased risk for multiple cancers was apparent in males, probably because of their higher level of daily smoking.
Project Dates:
1977–1982.
Financial Support:
University of California.
References:
(1) Silverman, S., Jr.; Greenspen, D.; Gorsky, M. "Tobacco Usage in Patients With Head and Neck Carcinomas: A Follow-Up Study on Habit Changes and Second Primary Oral/Oropharyngeal Cancers." *Journal of the American Dental Association* 106:33-35, January 1983. (2) Silverman, S., Jr.; Gorsky, M.; Lozada, F. "Oral Leukoplakia and Malignant Transformation. A Follow-Up Study of 257 Patients." *Cancer* 53(3):563-568, February 1, 1984.

0703. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, 1454 Fifth Avenue, San Francisco, California 94143.

Project Title:
Maintaining Non-Smoking.

Principal Investigators:
Hall, S.M.; Jones, R.T.
Objective:
To study methods to prevent relapse to smoking cigarettes.
Methods or Approach:
Behaviorally derived relapse prevention techniques were compared with an attention-placebo control. In a second study, 2 mg nicotine chewing gum was added to behavioral conditioning and this was compared with gum only and behavioral treatment only.

Results to Date:
Both large-scale studies have been completed.
Future Plans:
Placebo-controlled trials of behavioral treatment plus nicotine chewing gum and studies of cost-effective nicotine chewing gum treatment are planned.
Project Dates:
April 1980–continuing.
Financial Support:
NIDA (1R01 DA02538).

0704. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, LANGLEY PORTER NEUROPSYCHIATRIC INSTITUTE, 401 Parnassus Avenue, San Francisco, California 94143.

Project Title:
Neuropsychopharmacologic Studies of Tolerance and Dependence (Human).

Principal Investigator:
Jones, R.T.
Objective:
To investigate factors influencing tolerance and dependence on opiates, central nervous system depressants, cannabinoids, cocaine, tobacco, opiate-like peptides, and other drugs that may interact in clinical situations, and to determine the mechanisms and common effects between classes of drugs.
Methods or Approach:
Study emphasis is on hormones, cyclic nucleotides, and calcium as regulators. Novel treatments of dependence emphasize nonnarcotic treatment approaches and psychosocial interventions that change drug-seeking behavior. Naloxone-precipitated withdrawal following single doses of morphine is observed in normal and opiate-addicted volunteers. How caffeine, dexamethasone, and vasopressin modify the acquisition and expression of opiate dependence and psychological, physiological, and neurochemical effects of morphine and beta-endorphin will be measured. Measurement techniques to follow acute dependence and correlates of protracted abstinence in former opiate addicts will be refined. Measures of morphine effects and precipitated withdrawal include symptom and mood changes, cardiovascular and electroencephalographic responses, including auditory evoked late potentials in auditory signal detection tasks and vigilance tasks. Plasma ACTH, cortisol, vasopressin, and catecholamines will be measured to better compare animal and human models. Beta-endorphin will be compared with morphine.
Results to Date:
Results are not yet available.
Project Dates:
July 1977–June 1987.
Financial Support:
NIDA (5P01DA01696-06).

0705. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, LANGLEY PORTER PSYCHIATRIC INSTITUTE, 401 Parnassus Avenue, San Francisco, California 94143.

Project Title:
Tobacco Tolerance and Dependence (Human).

Principal Investigator:
Jones, R.T.
Objective:
To (1) determine the relative contribution of smoking patterns and metabolic factors on postsmoking blood levels; (2) investigate how a smoker obtains either the excitatory or relaxing effects of nicotine by altering puffing and inhalation patterns; and (3) clarify the role of nicotine in stress-induced smoking.
Methods or Approach:
Puff volume will be measured by a flowmeter and inhalation volume by inductance pneumography to provide a noninvasive and precise profile of how each cigarette is smoked on a puff-by-puff basis. Blood samples will be assayed for nicotine and cotinine by gas chromatography. Studies will involve several disciplines (psychopharmacology, psychophysiology, respiratory physiology, pharmacokinetics, and behavioral medicine) and may have direct public health implications by challenging the idea of a safe cigarette and emphasizing the smoker's role in determining nicotine and combustion product exposure levels. A detailed examination of smoking behavior in adolescent smokers may enhance prevention strategies.
Results to Date:
Results are not yet available.
Project Dates:
August 1978–August 1985.
Financial Support:
NIDA (5R01DA02088-07).

0706. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, 401 Parnassus Avenue, San Francisco, California 94143.

Project Title:
Marijuana Smoking Typography and Dose Regulation.

Principal Investigator:
Jones, R.T.
Objective:
To determine the extent and means by which people regulate tetrahydrocannabinol (THC) and other substances absorbed during marijuana smoking.
Methods or Approach:
Comparisons will be made between adolescent and adult marijuana smokers, frequent and infrequent users, males and females, and tobacco users and nonusers, to demonstrate the techniques, limits, and magnitude of dose regulation while smoking marijuana of various potencies. Reliable measurement techniques will be applied to cannabis dosimetry research. Puffing and inhaling patterns, including puff volume measured by flow meter techniques and inhalation volume measured by induction pneumography, will provide a noninvasive and precise profile of how each cigarette is smoked on a puff-by-puff basis. Cardiovascular, autonomic, and subjective effects and plasma THC, 11-hydrozy THC, 11-nor-9-carboxy THC, and carboxyhemoglobin measurements will allow determination of relationships between smoking patterns, resulting blood levels, and effects. Propranolol-induced beta adrenergic blockade and resulting changes in smoking behavior will examine the importance of autonomic system feedback in dose regulation. Detailed examination of marijuana smoking behavior in adolescent smokers may enhance prevention strategies.
Results to Date:
Results are not yet available.
Financial Support:
NIDA (1R01DA03473-01).

0707. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, CENTER FOR SOCIAL AND BEHAVIORAL SCIENCES, 1350 Seventh Avenue, San Francisco, California 94143.

Project Title:
Social and Pharmacological Factors in the Modification of Smoking Behavior.

Principal Investigators:
Hall, S.M.; Ginsberg, D.
Objective:
To develop a short-term intervention that can be used in outpatient health care settings; investigate effects of nicotine chewing gum and partner support in promoting abstinence following smoking cessation.
Methods or Approach:
A primary component of the program under development is a series of partner support training sessions. Abstinence rates of smokers who participate in treatment with partner-support training will be compared with abstinence rates for smokers who participate without partner-support training. Subjects will be randomly assigned within stratified blocks to treatment condition, based on self-selected nicotine gum use.
Results to Date:
Project is in a preliminary phase.
Project Dates:
July 1983–June 1986.
Financial Support:
ACS.

0708. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, Department of Pharmaceutical Chemistry, San Francisco, California 94143.

Project Title:
The Pharmacological Role of Nicotine in Humans.

Principal Investigators:
Castagnoli, N., Jr.; Trevor, A.J.
Objective:
To examine the oxidative metabolism of nicotine in human tissues; characterize potential bioactivation pathways that may relate to the carcinogenic properties of tobacco smoke condensate.
Methods or Approach:
High specific activity tritium-labeled nicotine will be incubated with various tissue preparations and extent of binding and metabolism will be monitored. Urine obtained from humans who have received nicotine will be examined for conjugates derived from potential reactive metabolites.
Results to Date:
Metabolism-dependent binding of tritiated S-nicotine (10 mCi/mmol) has been established in human and rabbit liver microsomal preparations. The extent of binding correlated with cytochrome P-450 levels and production of nicotine $\Delta^{1',5'}$-iminium ion metabolite (as measured by $\Delta^{4',5'}$-enamine formation). Such covalent binding may have relevance to toxic mechanisms underlying tobacco-related diseases.
Future Plans:
Studies will analyze human and animal lung preparations to assess the potential of target tissues to bioactivate nicotine. In vivo autoradiographic studies in rats are planned to identify possible regions of bioalkylation in the lung.
Project Dates:
July 1983–June 1986.
Financial Support:
NCI (CA 35678).

0709. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, Cardiology Division, 1186M, San Francisco, California 94143.

Project Title:
Effects of "Death in the West" on Children's Attitudes and Smoking Behavior.

Principal Investigator:
Glantz, S.A.
Objective:
To quantify the effects of seeing the film "Death in the West" in various settings and in combination with a supplementary curriculum on children's attitudes toward smoking and smoking behavior; investigate effects on perceptions of cigarette advertising in general and the Marlboro cowboy in particular.
Methods or Approach:
Surveys were conducted before and after seeing the film and completing the curriculum. Short-term followup has been conducted, but a long-term followup would be desirable.
Results to Date:
The film significantly reduces the credibility of cigarette advertising in general and the appeal of the Marlboro cowboy in particular. This latter finding is especially significant because Marlboro is the most popular cigarette among children.
Future Plans:
A new film and curriculum will be developed to follow the current one. The new package will be focused on involuntary (passive) smoking.
Project Dates:
April 1983–continuing.

0710. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, Cardiology Division, 1186M, San Francisco, California 94143.

Project Title:
Ongoing Bibliography on Involuntary Smoking.

Principal Investigators:
Glantz, S.A.; Jensen, L.
Objective:
To maintain a current bibliography of scientific papers published on the nature and health effects of involuntary smoking.
Methods or Approach:
Standard bibliographic techniques are used to compile the bibliography.
Results to Date:
A bibliography of about 500 papers has been created.
Future Plans:
The bibliography will be maintained and expanded as more papers are published.
Financial Support:
University of California, San Francisco.

0711. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, NORTHERN CALIFORNIA CANCER PROGRAM, 1801 Page Mill Road, Building B, Suite 200, Palo Alto, California 94304.

Project Title:
Mutagenic Cervical Mucus in Women Smokers.

Principal Investigators:
Holly, E.A.; Petrakis, N.
Objective:
To determine whether any association exists between mutagen-

icity of a woman's uterine cervical mucus and current smoking status.

Methods or Approach:

Cervical fluids were obtained from 78 premenopausal women seen between July 1983 and March 1984 at the University of California dysplasia and diethylstilbestrol clinic or in a private practice. Women were interviewed with regard to smoking and reproductive histories. Cervical fluids were tested for mutagenicity using the Ames/Salmonella microsomal test.

Results to Date:

Positive tests were found for 14 of 36 current smokers (39 percent) compared with 5 of 42 nonsmokers (12 percent). The odds ratio estimate (OR) was 4.7. Secretions from 13 of 31 women who had smoked within the previous 6 hours were positive on the laboratory test. Among women who had smoked ≥ 7 hours before specimens were obtained, one of five tested positively (OR, 2.9). Fluids from women with dysplasia or carcinoma in situ were more likely to be mutagenic than fluids from other women (OR, 2.0). The relationship between smoking and mutagenic cervical fluids offers biochemical evidence for the association (already noted in previous epidemiologic studies) between cervical cancer and cigarette smoking.

Future Plans:

Preliminary findings were based on small numbers and were not adjusted for variables that may be associated with mutagenic cervical fluids; however, it is unlikely that the variables could account for the strong positive association noted. A larger study is anticipated to investigate the relationship of mutagenicity of cervical fluids to smoking history, sexual and reproductive factors, and dietary exposures to possible mutagens.

Project Dates:

July 1983–December 1984.

Financial Support:

University of California, San Francisco; Northern California Cancer Program (P30CA 19408, P01 CA 13556-13).

0712. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, Department of Medicine, Division of General Internal Medicine, 400 Parnassus Avenue, San Francisco, California 94143.

Project Title:

Physician Counseling for Smoking Cessation.

Principal Investigators:

Coates, T.J.; Cummings, S.R.; Martin, A.R., et al.

Objective:

To develop a comprehensive program to help physicians advise smokers to quit.

Methods or Approach:

The program includes (1) a seminar that will teach physicians about smoking cessation, using role-playing to improve their advice; (2) office-based counseling that identifies smokers by an intake questionnaire about smoking habits and smoking-related symptoms; (3) individualized counseling by physicians about the benefits of quitting; (4) prescription from the physician for a date to quit; (5) booklet about quitting; and (6) instructions for physicians and patients in appropriate use of nicotine gum. To minimize relapse, patients will make a 1-month followup visit to reinforce motivation to quit, and will learn skills to stay abstinent. To encourage physicians to continue to advise smokers, the program will include "booster" conference calls between physicians and seminar instructors, a cumulative log of smokers who have accepted dates to quit, and postcards from patients who have successfully quit. A randomized trial will test the hypothesis that physicians who receive the program will achieve significantly higher long-term abstinence rates among patients who smoke than those who do not receive the program. Physicians in private practice in San Francisco (100) and internists from six Kaiser Permanente Medical Groups (100) will be randomly allocated to receive the program or serve as controls. Twenty smokers randomly drawn from each physician's practice will be interviewed about smoking habits 12 and 24 months after entry into the study. Expired carbon monoxide and saliva thiocyanate will be measured to verify abstinence. Efficacy in different subgroups of physicians and patients will be analyzed. Predictors of physician efficacy in counseling and of patient success in quitting will be identified, and changes in physicians' knowledge, attitudes, and behavior resulting from seminar attendance will be described.

Results to Date:

Project is in a preliminary phase.

Project Dates:

July 1984–June 1989.

Financial Support:

NCI (1R01CA38374).

0713. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, INSTITUTE OF HEALTH POLICY STUDIES, 1326 Third Avenue, San Francisco, California 94143.

Project Title:

Developing an Intervention Strategy for Pregnant Smokers.

Principal Investigator:

Wilner, S.

Objective:

To develop and evaluate a strategy to intervene with pregnant smokers who receive prenatal care at the Neighborhood Health Centers in Massachusetts.

Methods or Approach:

The project developed a strategy for needs assessment by surveying providers and patients, and conducting site visits to individual health centers. The strategy includes conducting a training seminar for physicians and nurses to teach them how to counsel patients, and developing patient guides to reinforce provider's messages, waiting room materials, and physician/nurse protocol to be used at each prenatal visit. Two centers have been selected for testing the strategy; two matched sites will serve as controls. Centers represent different patient populations. Evaluation criteria includes provider evaluations of the seminar and protocol of the 10-month trial. In this short time frame, cessation rates cannot be determined, but 1-year followup is anticipated.

Results to Date:

Results are not yet available.

Project Dates:

September 1984–July 1985.

Financial Support:

Massachusetts Department of Public Health.

0714. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, Department of Oral Medicine and Hospital Dentistry, San Francisco, California 94143.

Project Title:

Oral Leukoplakia and Malignant Transformation. A Follow-Up Study of 257 Patients.

Principal Investigators:

Silverman, S., Jr.; Gorsky, M.; Lozada, F.

Objective:
To update followup on a group of leukoplakia patients observed for a number of years; describe clinical characteristics and associated factors in progression and malignant transformation of this condition.
Methods or Approach:
The cohort consisted of 257 patients with oral leukoplakia who were studied and followed for an average of 7.2 years. All lesions were >1 cm in size and had been present and observed for a minimum of 6 months. Of initial biopsies, 235 revealed a benign hyperkeratosis and 22 contained some degree of epithelial dysplasia. Among all patients, 73 percent used tobacco, with cigarette usage the predominant form.
Results to Date:
Squamous carcinomas in the hyperkeratotic epithelial site subsequently developed in 45 patients (17.5 percent) in an average time of 8.1 years. Eight were in patients who originally had had epithelial dysplasia. High risks for malignant transformation also included nonsmoking patients, clinical presence of erythroplasis (erythroleukoplakia), and a clinical verrucous-papillary hyperkeratotic pattern. Duration of leukoplakia progressively increased total number of malignant transformations, with the highest rate occurring in the second year. Data confirm that oral leukoplakia is a precancerous lesion and that certain characteristics indicate greater risks and warrant consideration of more aggressive management.
Financial Support:
NCI (CA 17914-08).
Reference:
Silverman, S., Jr.; Gorsky, M.; Lozada, F. "Oral Leukoplakia and Malignant Transformation. A Follow-Up Study of 257 Patients." *Cancer* 53:563-568, 1984.

0715. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, SCHOOL OF DENTISTRY, Department of Oral Medicine and Hospital Dentistry, San Francisco, California 94143.

Project Title:
Tobacco Usage in Patients With Head and Neck Carcinomas: A Follow-Up Study on Habit Changes and Second Primary Oral/Oropharyngeal Cancers.

Principal Investigators:
Silverman, S., Jr.; Gorsky, M.; Greenspan, D.
Objective:
To reexamine the risk of tobacco usage and its association with development of multiple oral/oropharyngeal carcinomas.
Methods or Approach:
The study group consisted of 160 patients with head and neck carcinomas whose inclusion was contingent on a biopsy-proved carcinoma, recording of tobacco usage, and a minimum guarantee of a 1-year followup examination after treatment of the malignancy. A second primary cancer was recorded only if it occurred in an oral/oraphyaryngeal site different from the first primary lesion, thus virtually eliminating confusion with recurrence of the first primary cancer. Among the 90 males and 70 females, 73 percent used tobacco, and 87 percent of users smoked cigarettes (almost all more than a pack/day). Approximately the same percentage of men and women smoked (74.4 percent and 71.4 percent, respectively), although men usually consumed more cigarettes/day than women.
Results to Date:
Data indicate that patients who do not change smoking habits are at increased risk and confirms the high risk relationship between tobacco use and development of second primary malignancies of the oral/oropharyngeal area. The most critical factor relating to carcinogenesis appears to be the level of smoking. There is probably a critical carcinogenic threshold for tobacco usage in each individual in whom a malignancy developed; therefore, reducing tobacco use appeared to have almost the same effect as in those who discontinued smoking altogether or who had never smoked. The slight increase in second primary cancers among males appeared to be related to heavier tobacco use.
Financial Support:
NCI (CA 17914-07).
Reference:
Silverman, S., Jr.; Gorsky, M.; Greenspan, D. "Tobacco Usage in Patients with Head and Neck Carcinomas: A Follow-Up Study on Habit Changes and Second Primary Oral/Oropharyngeal Cancers." *Journal of the American Dental Association* 106:33-35, January 1983.

0716. UNIVERSITY OF CALIFORNIA, SANTA CRUZ, Santa Cruz, California 95064.

Project Title:
Examining the Mediating Role of Personality Variables on Environmental Factors: Testing a Theoretical Model of Adolescent Smoking Behavior.

Principal Investigator:
Burke, T.A.
Objective:
To investigate the influences of social environment and personality in the complex and dynamic process of the development of adolescent smoking behavior that will be useful to those interested in designing prevention programs.
Methods or Approach:
Seventh grade students (n = 1,400) from five public junior high schools will be administered a baseline questionnaire; the second survey will be carried out when students are finishing eight grade; the final survey will be made when the cohort is in the ninth grade. The specific variables in the survey instrument, which examines an interactive personality–environmental system, assess components that could possibly be affected in such a way as to decrease the likelihood of smoking; aspects of personality susceptible to educational influence (anxiety, self-esteem, approval seeking); and perceived social utility of smoking, peer group normative smoking behavior, quality of family life, need for autonomy, and traditional/nontraditional orientation. Data will be analyzed by comparing the model used with an unstructured simultaneous regression equation, and variances accounted for by the two methods will be examined. If the model accounts for significantly more variance than the atheoretical equation, results will shed light onto certain findings that will be of value in the design of more effective prevention efforts.
Project Dates:
July 1983–June 1985.
Financial Support:
California Research and Medical Education Fund; ALA, California.

0717. UNIVERSITY OF SAN FRANCISCO, INSTITUTE OF CHEMICAL BIOLOGY, 2130 Fulton Street, San Francisco, California 94117-1080.

Project Title:
Intratracheal Administration of Hydrocarbons.

Principal Investigator:
Furst, A.

Objective:
To determine the relative potency of hydrocarbons administered endotracheally in various mouse strains.
Methods or Approach:
Hydrocarbons are suspended in 0.2 percent gel in 0.9 percent saline and instilled into the lungs of specific strains of mice. At times, asbestos or another carrier is mixed with the hydrocarbon suspension (or administered before). Animals are then kept until loss of weight is noted; they are then sacrificed and a necropsy is performed. Lungs are preserved in the inflated state. Histological slides are made of the lungs and all suspicious tissues. Diagnosis of pathology is made by the consulting pathologist.
Results to Date:
3-Methylcholene (3-MC) is more potent than benzo(*a*)pyrene (BaP) or dimethylbenzanthracene (DMBA) as an inducer of lung tumors in mice. The relative order of toxicity is 3-MC > DMBA > > BaP. BaP induces squamous metaplasia but not carcinoma if no carrier is used. 3-MC does induce squamous cell carcinoma while DMBA is quite toxic.
Project Dates:
1975–December 1985.
Financial Support:
University of San Francisco.

0718. UNIVERSITY OF SOUTHERN CALIFORNIA, 222 North Grand Avenue, Los Angeles, California 90012.

Project Title:
Cardiovascular Fitness and Other Risk Factors.

Principal Investigator:
Cady, L.D.
Objective:
To use prospective population data on physical work capacity, cholesterol, blood pressure, and smoking to test the hypothesis that physical work capacity is protective against subsequent myocardial infarction.
Methods or Approach:
A prospective epidemiologic study was conducted with firefighters and law enforcement personnel in a classic examination and followup investigation of coronary heart disease.
Results to Date:
Individuals with high physical work capacity (above the 50th percentile) had half the incidence of subsequent myocardial infarction of individuals with low physical work capacity ($p < 0.05$). The protective effect persisted after adjusting for smoking, blood pressure, cholesterol, and age. Protection is sixfold if two other risk factors co-exist.
Future Plans:
The effect of changes in risk factors on changes in cardiovascular first event morbidity will be evaluated.
Project Dates:
1971–1986.
Financial Support:
University of Southern California; NHLBI (18235).

0719. UNIVERSITY OF SOUTHERN CALIFORNIA, SCHOOL OF MEDICINE, 2025 Zonal Avenue, Los Angeles, California 90033.

Project Title:
Atherosclerosis Progression and Regression.

Principal Investigator:
Blankenhorn, D.H.
Objective:
To determine the influence of cigarette smoking on femoral and coronary artery lesion change in human subjects.
Methods or Approach:
The subjects, men aged 40 to 59 who have had coronary bypass surgery, will have coronary angiography and femoral angiography. Approximately 80 smokers and 80 nonsmokers will be entered into separate treatment groups randomized between diet therapy or diet therapy plus Colestid and niacin. It is anticipated that a 30 percent difference in cholesterol level will exist between the drug-treated and nontreated groups. Urinary nicotine excretion levels will be studied at intervals.
Results to Date:
Results are not yet available.
Project Dates:
July 1979–June 1984.
Financial Support:
NHLBI (HL 23619-06).

0720. UNIVERSITY OF SOUTHERN CALIFORNIA, SCHOOL OF MEDICINE, 2025 Zonal Avenue, Los Angeles, California 90033.

Project Title:
Case–Control Study of Cancers of the Nose, Sinus, and Nasopharynx.

Principal Investigator:
Preston-Martin, S.
Objective:
To (1) investigate the association between cancers of the nose and nasopharynx and occupational exposure to dust, smoke, and fumes; (2) identify high-risk occupations and industries; and (3) investigate the relationship of these cancers to tobacco and alcohol use and to a history of upper respiratory infection or irritation.
Methods or Approach:
The case–control study is conducted by telephone interview. Eligible cases include non-Oriental men and women who are ages 25 through 69 with a cancer of the nose, sinus, or nasopharynx diagnosed from 1979 to the present (new cases diagnosed through 1984 will be included). All cases must be alive and able to be interviewed in English. Cases are identified by the Los Angeles County/University of Southern California Cancer Surveillance Program. A neighbor control of like sex, race, and age (birthyear within 5 years) will be selected for each case. The questionnaire used in the interview elicits detailed histories of job experiences, upper respiratory disorders, and tobacco use.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1982–1987.
Financial Support:
ACS.

0721. UNIVERSITY OF SOUTHERN CALIFORNIA, SCHOOL OF MEDICINE, Department of Family and Preventive Medicine, 2025 Zonal Avenue, Los Angeles, California 90033.

Project Title:
Epidemiology of Tumors of the Parotid Gland.

Principal Investigators:
Preston-Martin, S.; Yu, M.C.; Henderson, B.E.
Objective:
To test the hypothesis that previous exposure to diagnostic

dental x rays and to other forms of radiation are causally related to tumors of the parotid gland; evaluate the importance of other potential risk factors for this disease.

Methods or Approach:

Cases include all types of parotid neoplasms (both benign and malignant) identified by the Los Angeles County/University of Southern California Cancer Surveillance Program over a 5 year period. A neighbor control of like sex, race, and age (birth year within 5 years) will be selected for each case. Information on dental and medical x rays, job exposures, family cancers, and tobacco and alcohol use will be obtained through telephone interviews using a standard questionnaire. Interview information on dental x rays will be validated for a subset of cases and controls by a review of dental records. The relative importance of various exposures at different ages will be evaluated. Associations of tumor occurrence with radiation exposure and with smoking history will be analyzed separately for tumors of different histologic types.

Results to Date:

Results are not yet available.

Project Dates:

July 1980–continuing.

Financial Support:

NCI (R01 CA 28215-02).

0722. UNIVERSITY OF SOUTHERN CALIFORNIA, SCHOOL OF MEDICINE, 2025 Zonal Avenue, Los Angeles, California 90033.

Project Title:

Interaction of Cigarette Smoking and Air Pollution in Causing Airway Obstruction.

Principal Investigators:

Kilburn, K.H.; Warshaw, R.; Thornton, J.C.

Objective:

To determine contribution of cigarette smoking, ambient air pollution (smog), and occupational exposure (particularly asbestos and welding fumes) to airway obstruction.

Methods or Approach:

Cross-sectional studies in the Los Angeles basin are being conducted to determine whether nonsmokers without occupational exposure (persons in households of shipyard workers) have reduced midflow (FEF$_{25-75}$) and terminal flow (FEF$_{75-85}$). Smoking-specific comparisons permit calculation of relative contributions of cigarette smoking, air pollution, and specific occupational exposures. Longitudinal studies will show progression across intervals, and by comparing nonsmokers with smokers, will permit estimation of the type of interaction (additive, synergistic, or antagonistic).

Results to Date:

Among 414 women without occupational exposure, there was significant reduction in terminal and midflow and impaired distribution of gas as shown by diffusing capacity for carbon monoxide. Cigarette smokers had even greater reductions. Low exposure to asbestos in households of shipyard workers did not affect the relationships, and shipyard workers showed less flow reduction. It is suggested that exposure to asbestos produced peribronchiolar fibrosis, which may have opposed the obstruction due to cigarette smoke and air pollution. Only 20 percent of the workers continue to smoke (less than half the national average), down from an earlier 83 percent.

Future Plans:

A longitudinal study of the entire cohort will be conducted after a 4-year interval, and smoking behavior will be examined in detail.

Project Dates:

January 1981–January 1986.

Financial Support:

University of Southern California; NCI; ALA.

0723. UNIVERSITY OF SOUTHERN CALIFORNIA, SCHOOL OF MEDICINE, 2025 Zonal Avenue, Los Angeles, California 90033.

Project Title:

Effect of Smoking and Air Pollution on Asthma and Airway Function in Los Angeles School Children.

Principal Investigators:

Kilburn, K.H.; Warshaw, R.; Thornton, J.C.

Objective:

To (1) measure prevalence of asthma in second and fifth grade schoolchildren; (2) examine children for wheezing and flow rates and response to bronchodilator by spirometry; and (3) verify cigarette smoking and exposure to ambient air pollution by measuring alveolar carbon monoxide levels.

Methods or Approach:

More than 1,200 children of both sexes, from three major ethnic groups (latino, black, white), in second and fifth grade from eight Los Angeles schools have been evaluated. Parental and student questionnaires were administered; chest examination and spirometry at baseline and after bronchodilator were recorded in the spring of 1984. Alveolar carbon monoxide (after 20 seconds of breath holding) was also measured.

Results to Date:

Second-grade children had significantly higher self-reported wheezing and shortness of breath together with a higher prevalence of 20 percent improvement in forced expiratory flow (25-75 percent) or 10 percent improvement in forced expiratory volume in 1 sec than students in fifth grade. Less than 1 percent of the second graders smoked cigarettes. Carbon monoxide (CO) levels reflected home exposure (household smoking) and ambient CO as a component of air pollution. Ethnic differences were suggested, particularly lower function with lower responsiveness to bronchodilators in blacks. Further analyses will be made of the data collected.

Future Plans:

Interval changes at 1 year in baselines and bronchodilator responses will be studied.

Project Dates:

January 1984–January 1986.

Financial Support:

NCI.

0724. UNIVERSITY OF SOUTHERN CALIFORNIA, HEALTH BEHAVIOR RESEARCH INSTITUTE, 1985 Zonal Avenue, Los Angeles, California 90033.

Project Title:

Television Smoking and Family Project.

Principal Investigators:

Flay, B.R.; Hansen, W.B.; Johnson, C.A., et al.

Objective:

To determine the optimal combination of media and classroom instruction emphasizing social resistance training and family-oriented smoking prevention/cessation for seventh grade students and parents who smoke.

Methods or Approach:

The study consists of a 2 X 2 factorial design: television or not by classroom instruction or not. It will be conducted as an efficacy trial to test the relative effectiveness of program components implemented under optimal conditions. Junior high school complexes will be assigned randomly to experimental conditions from matched clusters. Measurement of student/parent knowledge, attitudes, social normative beliefs, self-efficacy, smoking behavior, and intended behavior will be obtained at pretest, immediately posttest, and at 6-month, 1-year, and 2-year followup.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Project results will contribute to data base for subsequent cigarette and related drug abuse prevention/cessation research.

Project Dates:
September 1984–August 1989.

Financial Support:
NIDA; KABC Television; Feeling Fine Production Company.

0725. UNIVERSITY OF SOUTHERN CALIFORNIA, HEALTH BEHAVIOR RESEARCH INSTITUTE, 1985 Zonal Avenue, Los Angeles, California 90033.

Project Title:
Comprehensive Television and Smoking Prevention/Cessation Utilizing School and Family-Oriented Social Resistance Skills Training.

Principal Investigators:
Flay, B.R.; Johnson, C.A.; Hansen, W.B.

Objective:
To assess the relative efficacy of a smoking prevention program that combines classroom instruction with a television component and a television-only program (factors include students' smoking behavior and knowledge, attitudes, and beliefs about substance abuse); reduce incidence of habitual cigarette smoking in seventh grade students and thereby the risk of smoking-related cancers.

Methods or Approach:
In the Los Angeles area, 50,000 seventh grade students received a classroom smoking prevention curriculum and media component utilizing social resistance training. The media component, produced by KABC, was aired in two parts: five 5-minute segments on local news program covered prevention, and five covered cessation. Students in the treatment condition were encouraged to view the programs with their parents. Students from matched schools provided a control comparison. A third group, in an encouragement-only condition, did not receive the classroom component, but were encouraged to view the media program. Data were collected at baseline, immediately after treatment, and at 1 and 2 years following treatment.

Results to Date:
Results indicated that 63 percent of the students who received classroom instruction viewed one or more of the prevention segments. Of these, 67 percent reported viewing the program with someone else and 71 percent reported talking about the program with others. Treatment students were only two-thirds as likely to have tried their first cigarette between pretest and posttest as control students. Level of viewing and parental participation were found to be related to program effectiveness. Teacher training had a significant effect on most outcomes. All effects were maintained at followup. Results led to the development of a recently funded, second-phase prevention/cessation project, the "Television Smoking and Family Project."

Financial Support:
KABC Television; Feeling Fine Production Company.

0726. UNIVERSITY OF SOUTHERN CALIFORNIA, HEALTH BEHAVIOR RESEARCH INSTITUTE, 1985 Zonal Avenue, Los Angeles, California 90033.

Project Title:
Project PASS UP: Parents and Students Substance Use Prevention.

Principal Investigators:
Grossman, L.M.; Flay, B.R.

Objective:
To test effectiveness of parental participation in a school-based prevention program in reducing onset rates of tobacco, alcohol, and marijuana use.

Methods or Approach:
Project PASS UP is a prospective longitudinal study of 1,600 seventh graders from six program schools and four control schools, matched for race and socioeconomic status. Program schools received a 10-day substance abuse prevention curriculum that focused on skills to resist substance use. Half the program schools were randomly assigned to the High Parent Involvement (HPI) condition in which students and parents were given extra incentives to complete homework activities together. The Low Parent Involvement condition received no special encouragement. Self-report and biological measures of substance use were collected at pretest, immediately posttest, and 6 and 18 months following program implementation.

Results to Date:
Results at 6-month followup showed significant differences between program and control schools on intentions, attitudes, and actual substance use behaviors. Students who received the program were less likely to use, or intend to use, alcohol, tobacco, or marijuana. When parents were more involved in the program, students indicated greater confidence in talking to their parents about drugs, practicing assertiveness, and refusing drug offers. At pretest, specific risk factors were found that predicted future onset of substance use 6 months later.

Future Plans:
Data from 18-month followup are being analyzed to determine if effects persist, or as anticipated, become stronger as natural onset rates begin to increase.

Project Dates:
April 1982–January 1985.

Financial Support:
ALA.

0727. UNIVERSITY OF SOUTHERN CALIFORNIA, HEALTH BEHAVIOR RESEARCH INSTITUTE, 1985 Zonal Avenue, Los Angeles, California 90033.

Project Title:
Project Smart.

Principal Investigators:
Johnson, C.A.; Flay, B.R.; Hansen, W.B.

Objective:
To (1) reduce the incidence of habitual cigarette smoking and alcohol and marijuana abuse in sixth, seventh, and eighth grade students; (2) evaluate relative effectiveness of two intervention strategies based on social developmental theories in terms of reduced rates of substance use and abuse; and (3) determine relative effectiveness of comparable interventions made at different stages of adolescent development in terms of reduced rates of substance use and abuse.

Methods or Approach:
Two curricula, based on social resistance training (social learning and self-management), are being implemented (using a stratified sampling technique) in Los Angeles public schools

over a 4-year period. Matched schools have been identified as controls. Individuals from each cohort are measured at baseline and followed throughout the 5-year study. Complete and developmental cohorts have been identified. Students in the complete condition receive the program during one semester; student in the developmental condition receive the program in small increments over a 3-year period.

Results to Date:
Results from the first year of intervention demonstrate that drug use increases dramatically between sixth and seventh grades. A social resistance curriculum can be very effective in reducing incidence of substance use 1 year later. However, a curriculum that deals with personal control and self-management was not an effective teaching tool for prevention. A test of a combined social resistance and self-management curriculum is now underway. Cross-sectional data show that students use different substances for similar reasons. The same model of influence appears to fit students' use of cigarettes, alcohol, and marijuana. Process measures indicate that students in treatment conditions who were taught by Project health educators were better able to demonstrate skills and recall information than students taught by public school teachers.

Project Dates:
March 1982–February 1987.

Financial Support:
NIDA.

0728. UNIVERSITY OF SOUTHERN CALIFORNIA, HEALTH BEHAVIOR RESEARCH INSTITUTE, 1985 Zonal Avenue, Los Angeles, California 90033.

Project Title:
School and Family Cancer Prevention Project.

Principal Investigators:
Johnson, C.A ; Flay, B.R.; Hansen, W.B., et al.

Objective:
To expand on a previously successful substance use prevention program (Project SMART) to test effects of breadth of program content and level of parent involvement in preventing cigarette smoking and other cancer-related behaviors among adolescents.

Methods or Approach:
In a 4-year, prospective longitudinal study, junior high schools will be randomly assigned to one of four program conditions or to the control condition and evaluated at yearly intervals for breadth of program content and level of parental involvement. Half of the program schools will receive a smoking prevention curriculum and half a more broadly oriented healthy lifestyles curriculum that incorporates alcohol and marijuana prevention and promotion of aerobic exercise and low-fat diet. Half of the schools in each group will be assigned to either the school-only condition (receiving standard curricula) or the school and parent condition, which includes active parent participation in homework and establishment of parent advocacy groups in the schools involved. Evaluation includes self-report measures, from students and parents, of dietary, exercise, and substance use behaviors and attitudes. Biological measures of height, weight, and ergometric fitness will be monitored on a random sample of classes.

Results to Date:
Project is still in the pilot stage, but preliminary studies of several process variables indicate high levels of parent participation in activities and enthusiastic ratings of the program from both parents and students. Full-scale implementation will begin in September 1985 and longitudinal evaluations will be conducted for 4 years.

Project Dates:
January 1984–January 1985.

Financial Support:
NCI.

0729. UNIVERSITY OF SOUTHERN CALIFORNIA, HEALTH BEHAVIOR RESEARCH INSTITUTE, 1985 Zonal Avenue, Los Angeles, California 90033.

Project Title:
Community Health Promotion Project (Pilot) to Reduce Substance Abuse, Including Cigarette Smoking, Among Adolescents.

Principal Investigators:
Johnson, C.A.; Flay, B.R.

Objective:
To assess the feasibility of implementing a substance abuse prevention program aimed at adolescents that incorporated active involvement of all elements of a community (schools, business and government, families, and the media).

Methods or Approach:
The concurrent approaches employed were (1) development of a coherent data- and theory-based program; (2) community organization to identify key community leaders; (3) coordination with schools; (4) mounting of a media campaign to raise awareness; (5) coordination of efforts with concerned parent groups; (6) involvement of local health professionals; (7) recruitment of voluntary activity community groups and churches; and (8) implementation of intensive and visible prevention efforts to raise awareness and provide education.

Results to Date:
Data are being analyzed. Preliminary findings suggest the capability of networking many levels of a community, although program dissemination requires a long period of time.

Future Plans:
Future plans are for a large-scale, long-term project involving experimental community and control sites for a substance abuse prevention program aimed at adolescents.

Project Dates:
June 1983–January 1985.

Financial Support:
William T. Grant Foundation.

0730. UNIVERSITY OF SOUTHERN CALIFORNIA, SCHOOL OF MEDICINE, 2025 Zonal Avenue, Los Angeles, California 90033.

Project Title:
Adenocarcinoma of the Lung in Females in Los Angeles Country.

Principal Investigators:
Yu, M.C.; Wu, A.H.; Henderson, B.E.

Objective:
To investigate the role of personal smoking, passive smoking, dietary intake of vitamin A, prior lung diseases, and use of fuels in etiology of adenocarcinoma of the lung in white females in Los Angeles County.

Methods or Approach:
Incident cases of adenocarcinoma of the lung in the case-control study were identified through the Los Angeles County Cancer Surveillance Program. Controls, matched for age and neighborhood, will be identified. Cases and controls will be interviewed in person using a structured questionnaire, modified from the pilot study to include more detailed information on suspected risk factors. It is anticipated that 350 case-control pairs will be interviewed.

Results to Date:
Results are not yet available.
Project Dates:
December 1983–December 1985.
Financial Support:
Margaret E. Early Medical Research Trust.

0731. UNIVERSITY OF SOUTHERN CALIFORNIA, SCHOOL OF MEDICINE, 2025 Zonal Avenue, Los Angeles, California 90033.

Project Title:
Case–Control Study of Carcinoma of the Lung in Women.

Principal Investigators:
Henderson, B.E.; Pike, M.C.; Wu, A.H.
Objective:
To investigate the role of personal smoking, passive smoking, prior lung diseases, and dietary consumption of vitamin A in the etiology of adneocarcinoma and squamous cell carcinoma of the lung in white females in Los Angeles County.
Methods or Approach:
Incident lung cancer cases were identified through the Los Angeles County Cancer Surveillance Program; controls were selected and matched for age and neighborhood. Cases and controls were interviewed by telephone using a structured questionnaire designed to elicit information on personal smoking habits, lifetime exposure to passive smoke, dietary intake of foods rich in vitamin A, and prior lung diseases.
Results to Date:
Personal cigarette smoking accounted for almost all of the 149 cases of adenocarcinoma and about half of the 71 cases of squamous cell carcinoma. Among nonsmokers, slightly elevated relative risks for adenocarcinoma were observed for passive smoke exposure from spouses and at work. Childhood pneumonia and childhood exposure to coal burning were additional risk factors for adenocarcinoma. For both cell types, increased risks were associated with decreased intake of beta-carotene foods, but not for total preformed vitamin A foods and vitamin supplements.
Future Plans:
As a result of findings of this pilot study, a new case–control study will further investigate the risk factors suggested.
Project Dates:
April 1981–December 1982.
Financial Support:
ACS (SIG-2).

0732. UNIVERSITY OF SOUTHERN CALIFORNIA, SCHOOL OF MEDICINE, 2025 Zonal Avenue, PMB B-304, Los Angeles, California 90033.

Project Title:
Case–Control Study of Primary Hepatocellular Carcinoma in Los Angeles County.

Principal Investigators:
Yu, M.C.; Henderson, B.E.
Objective:
To identify risk factors of hepatocellular carcinoma.
Methods or Approach:
Risk factors under study are hepatitis B virus infection, cigarette smoking, alcohol consumption, exposure to chemicals, and use of oral contraceptives in women. Cases are identified through the Los Angeles County/University of Southern California Cancer Surveillance Program. Eligibility criteria include age under 75 years at time of diagnosis, being black or white, and being willing to be interviewed. In-person interviews are conducted, and a blood sample is obtained to test for presence of HBsAg by radioimmunoassay. For each HBsAg-negative patient interviewed, 2 controls, matched on race, sex, age (within 5 years), and neighborhood of residence are similarly interviewed. It is expected that 180 cases and 230 controls will be interviewed over a 5-year period.
Results to Date:
Results are not yet available.
Project Dates:
April 1984–April 1989.
Financial Support:
ACS.

0733. UNIVERSITY OF SOUTHERN CALIFORNIA, SCHOOL OF MEDICINE, Department of Preventive Medicine, 2025 Zonal Avenue, Los Angeles, California 90033.

Project Title:
Collaborative Case Control Study of Brain Tumours in Children.

Principal Investigator:
Preston-Martin, S.
Objective:
To (1) evaluate the role of parental and childhood exposure to N-nitroso compounds; (2) quantify importance of known risk factors (ionizing radiation and genetic predisposition); and (3) explore the relation to other suggested risk factors including head trauma, barbiturates, and parental occupational exposures.
Methods or Approach:
In utero and perinatal experiences are of particular interest. In the case–control study, biological mothers of 1,000 children aged 0 to 19 years with a primary tumor of the brain or cranial meninges and of an equal or greater number of population controls will be interviewed. Factors studied will include personal and passive smoking exposures of children and their parents. The study is being sponsored by the International Agency for Research on Cancer in Lyons, France.
Results to Date:
Project is in a preliminary phase.
Project Dates:
1985–1990.
Financial Support:
University of Southern California.

0734. VETERAN'S ADMINISTRATION MEDICAL CENTER, ENZYMOLOGY RESEARCH LABORATORY, Department of Medicine (151F), Martinez, California 94553.

Project Title:
Circulating Pancreatic Proteases and Aortic Aneurysm in the Aged Heavy Smoker.

Principal Investigator:
Geokas, M.C.
Objective:
To evaluate the responsiveness and susceptibility of the exocrine pancreas to a physiological stimulus (secretin) in heavy smokers.
Methods or Approach:
Serum samples (5 mL) are obtained by venipuncture from heavy cigarette smokers after a 12-hour overnight fast. Blood is drawn 10 minutes before and 15, 30, and 60 minutes after i.v. injection of 75 clinical units of secretin. Cationic trypsin and elastase 2 levels are determined in serum by radioimmunoas-

say. Trypsin-inhibitory and elastase-inhibitory capacity are also determined, as are levels of α_1-protease inhibitor and α_2-macroglobulin. Data are compared with results from nonsmoking volunteers free of known cardiovascular or pancreatic disease. Nonsmokers also undergo the secretin stimulation test.

Results to Date:

Basal levels of amylase were found to be twice as high in smokers as in nonsmokers. Serum amylase increased 100 percent and serum cationic trypsin levels increased threefold to fivefold. Serum elastase 2 levels increased twofold in smokers following secretin injection. Little change in the parameters was noted in nonsmokers.

Future Plans:

Data will be collected from enough smokers to help clarify the role of the exocrine pancreas and its proteolytic enzymes to better understand the underlying causes of diseases with associated tissue destruction (e.g., aortic aneurysm and pulmonary emphysema).

Project Dates:

May 1984–December 1985.

Financial Support:

VA.

0735. VETERANS ADMINISTRATION MEDICAL CENTER, Long Beach, California 90822.

Project Title:

Comparison of Hypnotherapy With Systematic Relaxation in the Treatment of Cigarette Habituation.

Principal Investigator:

Schubert, D.K.

Objective:

To determine whether hypnosis is effective in the treatment of cigarette habituation.

Methods or Approach:

Volunteers who wanted to quit smoking (41 males and 46 females, aged 17 to 56 years) were randomly assigned to the experimental hypnosis group, the comparison relaxation group, or the waiting list control group. Smokers in the treatment groups attended four weekly, 50-minute, individual sessions. Four months after completion of treatment, smokers were administered a questionnaire and a hypnotic susceptibility scale.

Results to Date:

Smokers in the hypnosis group who were in the upper two-thirds of the group in terms of hypnotic susceptibility reduced cigarette consumption substantially more than smokers in the relaxation group who were in the upper two-thirds of the group in terms of hypnotic susceptibility. The hypnotic state appears to be therapeutic for individuals who can enter medium or deep states of hypnosis.

Reference:

Schubert, D.K. "Comparison of Hypnotherapy With Systematic Relaxation in the Treatment of Cigarette Habituation." *Journal of Clinical Psychology* 39(2):198-202, March 1983.

0736. VETERANS ADMINISTRATION MEDICAL CENTER, Brentwood Division, 691/B151D, Los Angeles, California 90073.

Project Title:

Stimulation, Sedation, and Cigarette Smoking.

Principal Investigators:

Jarvik, M.E.; Herskovic, J.E.; Rose, J.E.

Objective:

To investigate the more potent rewards of smoking, including anxiety relief, improvement of mood, and optimization of ability to perform complex tasks.

Methods or Approach:

By using various types of cognitive and noncognitive tasks, subjective arousal and stress are manipulated and effects of manipulation on amount smoked and nicotine preference are studied. Nicotine preference is measured using a smoke-mixing device developed in this laboratory. The effects of different doses of nicotine, given in controlled doses of smoke or transdermally, on stress, arousal, and aggression are also examined.

Results to Date:

Findings indicate that stress increases cigarette smoking as measured by number of puffs taken when allowed to smoke. It was also found that transdermal nicotine reduces cigarette craving and nicotine preference. Findings agree with other experimental and anecdotal reports that cigarette smoking increases during stress, and indicate that transdermally applied nicotine is a promising experimental technique and could some day be used as a smoking cessation aid.

Future Plans:

Experiments will explore usefulness and efficacy of transdermal nicotine, and effects of smoking and nicotine on irritability and aggression.

Project Dates:

October 1983–October 1986.

Financial Support:

VA, Medical Research Service.

0737. VETERANS ADMINISTRATION MEDICAL CENTER, WEST LOS ANGELES, Brentwood Division 691/B151D, Los Angeles, California 90073.

Project Title:

Scaling the Reinforcement Value of Cigarette Smoking.

Principal Investigators:

Rose, J.E.; Jarvik, M.E.

Objective:

To measure the reinforcing properties of nicotine; determine how these vary as a function of dose, deprivation state, and presence of conditioned reinforcing stimuli.

Methods or Approach:

Reinforcing value is measured using a smoke mixer that allows subjects to control nicotine delivery of each puff. Nicotine preference is measured after deprivation or satiation. Transdermal nicotine administration is used to dissociate sensory and pharmacologic effects, and local anesthesia of the respiratory tract is used to block chemosensory stimuli in smoke.

Results to Date:

Nicotine preference increases after a period of deprivation and decreases after satiation. Transdermal nicotine reduces cigarette craving and nicotine preference. Blockade of chemosensory stimuli in smoke reduces subjective satisfaction of smoking. Findings support the view that nicotine has both sensory and pharmacologic reinforcing actions.

Future Plans:

Satiety produced by different sizes of nicotine boli presented with a smoke delivery apparatus will be investigated and the relationship between nicotine tolerance and nicotine preference will be studied.

Project Dates:

October 1983–September 1986.

Financial Support:

NIDA (2R01DA02665).

0738. VETERANS ADMINISTRATION MEDICAL CENTER, 211 Main Street, San Francisco, California 94105.

Project Title:
Smoking and Atherosclerosis. (A) the Effect of Smoke Components on Platelet Function.

Principal Investigator:
Effeney, D.J.
Objective:
To (1) determine effects of nicotine (N) on platelet function and catecholamine release in man; (2) examine effects of pretreatment with N and carbon monoxide (CO) alone and in combination on the ability of the heart to produce prostacyclin; (3) examine effects in rabbits of N perfusion of the ventricular septum; and (4) correlate work performed with prostacyclin production.
Methods or Approach:
Platelet function and catecholamine release was studied in man during 60-minute infusions of normal saline and 1.5 mg/kg N. N concentrations were measured using gas liquid chromatography; platelet catecholamine concentrations were measured with radioenzymatic technique; and platelet function studies were performed using a modification of the turbimetric method of Born. A model was developed in the rabbit that allowed prolonged infusion of N with simultaneous exposure to CO. The effect of the two treatment modalities alone and in combination were studied on the ability of the heart to produce prostacyclin. The isolated perfused rabbit intraventricular septal model modified by Raffa was used to examine effects of N on work performed by the heart. Biological activity of prostacyclin was assessed by ability to inhibit ADP-induced platelet aggregation and 6 keto PGF-1-alpha radioimmunoassay.
Results to Date:
At levels of circulating N equivalent to that obtained from smoking in some human subjects, platelet count fall sharply. Hyperaggregability to ADP and epinephrine, confirmed in some animals, occurred, as did reduction in prostacyclin production by various chambers of the heart after pretreatment with N and an increase in prostacyclin production after 1 week pretreatment with CO or when CO and N were administered together. N was widely distributed in animal tissues and was concentrated in the aorta and in the heart to levels two to three times those found in circulating blood. Results are important in helping to establish pathogenesis of atherosclerosis and the relationship of smoking to its initiation and continued development.
Financial Support:
VA.

0739. VETERANS ADMINISTRATION MEDICAL CENTER, 3801 Miranda Avenue, Palo Alto, California 94304.

Project Title:
Medical-Behavioral Evaluation of Aversive Satiation in Smoking Abatement.

Principal Investigators:
Hall, R.; Sachs, D.P.
Objective:
To examine safety and efficacy of rapid smoking, an aversive smoking cessation technique; determine smoking cessation rates 1 year after treatment.
Methods or Approach:
Smoking cessation rates were determined by patient self-report and verified by serum nicotine and cotinine levels.
Results to Date:
Eighteen subjects started treatment and four dropped out before treatment was completed. Twelve months after treatment, 9 of 18 (50 percent) were still abstinent. A waiting list control group reported that 21 percent had quit in the 1-year interval, but some had quit as recently as 1 month before followup. Results compare favorably with published reports in the literature. Despite recent criticism of rapid smoking, it appears to be a safe and effective treatment when the original method is closely followed and proper medical precautions are taken.
Financial Support:
VA.

0740. VETERANS ADMINISTRATION MEDICAL CENTER, 3801 Miranda Avenue, Palo Alto, California 94304.

Project Title:
Mechanism of Nitric Oxide Activation of Guanylate Cyclase.

Principal Investigator:
Murad, F.
Objective:
To purify soluble and particulate guanylate cyclase from lung and liver to homogeneity; examine the enzyme's kinetic properties in the native state and with nitric oxide activation.
Methods or Approach:
Monoclonal antibodies have been developed to the enzyme for affinity purification procedures, development of a radioimmunoassay for the protein, and immunohistochemical localization. Enzyme turnover will be examined in cell cultures, and the effects of various hormones, drugs, nitric oxide, and tobacco smoke on guanylate cyclase turnover will be examined.
Results to Date:
The soluble enzyme has been purified; it is 150,000 daltons and composed of two subunits of similar size. Particulate guanylate cyclase has been purified about 10,000-fold, but is not pure. The particulate enzyme is about 200,000 daltons and is a glycoprotein.
Financial Support:
VA.

0741. VETERANS ADMINISTRATION MEDICAL CENTER, 3801 Miranda Avenue, Palo Alto, California 94304.

Project Title:
Two Phase Smoking Cessation.

Principal Investigators:
Phillips, M.A.; Hall, R.G.
Objective:
To (1) improve the therapeutic effectiveness of smoking cessation treatment; (2) determine whether combining a persuasive message with self-control techniques will make a more effective smoking cessation program than using either alone; and (3) investigate attitudinal and personality variables previously hypothesized to be related to health behaviors.
Methods or Approach:
The design is a 2 X 2 factorial (persuasive message by self-control techniques) resulting in four conditions. Treatment was conducted in groups of 10 to 15 subjects per instructor. Each group met for nine sessions over a 4 1/2-week period (10 hours of treatment). Data were collected at five points: before and

immediately after the first session, before the second session, at the end of the ninth session, and 1 month after the ninth session. Questionnaires were used to assess personality and attitudinal variables. Smoking rate and abstinence were based on subject report and to some extent corroborated by respiratory air measurements and friend and family reports.

Results to Date:
Usable data have been collected from over 200 participants; analysis is being conducted on results.

Financial Support:
VA.

0742. VETERANS ADMINISTRATION, 11301 Wilshire Boulevard, West Los Angeles, California 90073.

Project Title:
Comparison of Saphenous Vein and e-PTEE Grafts in Femoral Popliteal Bypass Procedures.

Principal Investigator:
Wilson, S.E.

Objective:
To compare e-PTEE with saphenous vein grafts in femoral popliteal bypass procedures.

Methods or Approach:
A randomized prospective comparison was done over a 3-year period, based on peripheral resistance as measured by AWR <0.3-0.4 and <0.3. Patients were randomly assigned e-PTEE or vein grafts. Postoperatively, patients were followed at 3-month intervals. Data recorded included age, presence of diabetes mellitus, vessel patency, symptoms, treadmill distance and AWRs, and smoking habits. The time to first occlusion of the graft was examined as a measurement of patency with the belief that it would prove a more sensitive index of graft performance.

Results to Date:
The cumulative patency rate for vein grafts was 73.1 percent at 6 months, 66.7 percent at 12 months, 62.6 percent at 24 months, and 50.5 percent at 36 months, and for PTEE grafts was 59.1 percent at 6 months, 43 percent at 12 months, 32.3 percent at 24 months, and 25 percent at 36 months ($p > 0.1$). In the 42 grafts placed in the above-knee position, the mean patency time (interval to first occlusion) of vein grafts was 44.5 months, but only 15.6 months for PTEE grafts ($p < 0.04$). In the 45 below-knee grafts, the mean patency time for vein grafts was 22.6 months vs. 10 months for PTEE grafts ($p > 0.5$). Neither preoperative walking distance, smoking history, nor distal vessel run-off correlated with graft patency. The presence of gangrene, however, significantly decreased the interval to first occlusion (229 days vs. 487 days; ($p < 0.001$).

Financial Support:
VA.

0743. VETERANS ADMINISTRATION, 11301 Wilshire Boulevard, West Los Angeles, California 90073.

Project Title:
Toxicological Implications of Coal Tar and Psoralen Use in Psoriasis.

Principal Investigators:
Wheeler, L.A.; Lowe, N.

Objective:
To investigate the possible percutaneous absorption of mutagens by patients receiving crude coal tar (CCT) and ultraviolet light.

Methods or Approach:
Urine samples were collected from nonsmoking volunteers and from smoking and nonsmoking psoriasis patients.

Results to Date:
This study demonstrated the percutaneous absorption of mutagens from CCT and indicated that its effects may not be limited to the skin.

Financial Support:
Veterans Administration.

0744. VETERANS ADMINISTRATION, 11301 Wilshire Boulevard, West Los Angeles, California 90073.

Project Title:
Psychophysiological Effects of Cigarette Smoking.

Principal Investigators:
Syndulko, K.; Boyd, G.M.; Maltzman, I.

Objective:
To (1) demonstrate that abstinent smokers will show relatively greater left than right hemisphere activity; (2) relate this to the discomfort and craving that they experience; and (3) show that one mechanism of smoking reinforcement is the restoration of balance between the hemispheres.

Methods or Approach:
Bilateral skin conductance and EEG will be recorded from smokers in conditions of smoking and abstaining from smoking. Recordings will be made while subjects sit quietly at rest, passively listen to novel and familiar tones, and engage in a task of counting tones. Similar recordings will be made from nonsmoker control subjects. Recordings will be analyzed to determine the effects of nicotine on lateral asymmetries and how smokers differ from nonsmokers in terms of relative cerebral activation. Possible sex differences in response to nicotine will also be studied.

Results to Date:
This study is in a preliminary phase.

Financial Support:
VA.

0745. VETERANS ADMINISTRATION, 11301 Wilshire Boulevard, West Los Angeles, California 90073.

Project Title:
Risk Factor Mediated Intima Damage and Atherosclerosis.

Principal Investigator:
Sieffert, G.F.

Objective:
To create experimental atherosclerosis in rats.

Methods or Approach:
Rats were exposed to mechanically smoked cigarettes, to streptozotocin plus a high-cholesterol diet, or to the high-cholesterol diet alone.

Results to Date:
Cigarette smoke inhalation caused arterial endothelium changes in rats exposed to mechanically smoked cigarettes. The changes observed, however, could not be recognized as lesions typical of atherosclerosis in man. Rats treated with streptozotocin developed experimentally induced diabetes. Arterial endothelial changes were observed but changes did not resemble the characteristics of diseased human arteries. The addition of 2 percent cholesterol to the rats' diet did produce lesions that appeared identical to those in humans. Nondiabetic rats fed the same diet did not develop lesions. It is concluded that it is possible to create experimental atherosclerosis in Sprague-Dawley rats by first inducing diabetes and after 2 weeks placing the rats on a 2 percent cholesterol diet. Lesions

appeared within 9 weeks, but continued to worsen throughout the course of the study. There was a direct relationship between the extent of diabetes (as determined by blood glucose levels) and the extent of atherosclerosis produced.

Financial Support:

VA.

0746. VETERANS ADMINISTRATION, 11301 Wilshire Boulevard, West Los Angeles, California 90073.

Project Title:

Neuroendocrine Effects of Nicotine and Carbon Monoxide in the Human.

Principal Investigators:

Wilkins, J.N.; Carlson, H.F., Jarvik, M.E., et al.

Objective:

To identify significant alterations in neuroendocrine function in humans following nicotine and/or carbon monoxide (CO) exposure from cigarette smoking.

Methods or Approach:

The protocol is logistically divided into two phases. In phase I, endocrine responses to nicotine after smoking two conventional cigarettes or two very-low-nicotine cigarettes are quantified; in phase II select levels of circulating hormones are determined following exposure to CO in combination with a fixed nicotine dose.

Results to Date:

Findings of phase I revealed significant changes in circulating levels of cortisol and GH from the nicotine; circulating levels of prolactin were moderately elevated. Correlations have been made with corresponding circulating nicotine levels and heart rate. Analysis of variance with repeated measures is the primary statistical tool. Phase II has not been completed.

Financial Support:

VA.

Reference:

Wilkins, J.N.; Carlson, H.E.; Vunakis, H., et al. "Cigarette Smoking Increases Circulating Levels of Cortisol, Growth Hormone and Prolactin: Correlates with Blood Nicotine." *Psychopharmacology* 78(4):305-308, December 1982.

0747. VETERANS ADMINISTRATION OUTPATIENT CLINIC, 425 South Hill Street, Los Angeles, California 90013.

Project Title:

Freedom From Smoking Clinic (American Lung Association).

Principal Investigators:

Wolfe, G.; Hedrick, B.; Baskin, A., et al.

Objective:

To help veteran patients and employees of the outpatient clinic quit smoking.

Methods or Approach:

The program used, developed by the American Lung Association, consists of seven sessions, the first three held at weekly intervals. Smokers are asked to quit completely by the third session. The fourth session is held 2 days later, and the fifth, 5 days later. The sixth session is the following week; the final session is 2 weeks later. The sessions consists of lecture, movies, and open discussion; printed materials are available. Client participation is strongly recommended.

Results to Date:

The first "Freedom From Smoking" clinic (July-September 1983) averaged nine patients at each session. Five continue to be abstinent. Average attendance at the second clinic was eight employees; three or four continue to be nonsmokers. Of the eight veterans in the third clinic, five continue to abstain from smoking. The fourth clinic (August-October 1984) for 12 patients and employees, was less successful; only 6 finished the program, of which 3 are still abstinent.

Future Plans:

In the next clinic for veteran patients, nicotine chewing gum will be added to the program. Three or four clinics will be held each year.

Project Dates:

1983–continuing.

Financial Support:

VA.

0748. WADSWORTH VETERANS ADMINISTRATION MEDICAL CENTER, Wilshire and Sawtelle Boulevards, Los Angeles, California 90073.

Project Title:

Duodenal Mucosal Injury and Defense: Role of Blood Flow.

Principal Investigators:

Guth, P.H.; Leung, F.W.

Objective:

To determine (1) pattern of change in duodenal mucosal blood flow in various forms of experimental duodenal mucosal injury; (2) effect on duodenal mucosal blood flow of agents known to protect against or aggravate experimental duodenal mucosal injury; (3) relation between duodenal bicarbonate secretion and blood flow; and (4) effect of perfusion of the duodenal lumen with hydrochloric acid (HCl) on duodenal mucosal blood flow.

Methods or Approach:

Duodenal mucosal blood flow is measured by hydrogen gas clearance technique using platinum contact electrodes and 3 percent hydrogen in air. Administration of cigarette smoke is by a glass cylinder fitted over the snout and tracheostomy of anesthetized rats. The smoke is delivered into the cylinder via a side hole. For acid-induced duodenal mucosal injury, the duodenum is perfused with 0.1 N HCl via a PE90 tube passed through the stomach into the duodenum and secured at the pylorus.

Results to Date:

Tobacco smoke with nicotine (but not nicotine-free smoke) induced a significant decrease in duodenal mucosal blood flow; i.v. nicotine also induced dose-related reductions in blood flow. Nicotine-related decreases in duodenal mucosal blood flow may contribute to the susceptibility of the duodenum of cigarette smokers to acid peptic injury. It is concluded that cigarette smoke increases susceptibility of the duodenal mucosa to acid-induced injury by at least two mechanisms: nicotine-related (associated with reduction in blood flow) and nonnicotine-related (not associated with reduction in duodenal mucosal blood flow).

Future Plans:

Future research will study the effect of alpha adrenergic blockade on the adverse effect of cigarette smoke and i.v. nicotine on duodenal mucosal blood flow and injury.

Project Dates:

December 1983–November 1987.

Financial Support:

NIAMDD (27465); VA.

0749. WESTERN INSTITUTE OF BEHAVIORAL RESEARCH, 25 Center Street, Redlands, California 92373.

Project Title:
Cessation of Tobacco Mastication With Valeric Acid Olfactory Aversion/Covert Sensitization Procedures.

Principal Investigators:
Hart, R.R.; McNeill, J.

Objective:
To evaluate and assess utility of an olfactory aversion/covert sensitization procedure in cessation of tobacco chewing.

Methods or Approach:
A pilot inquiry, employing an ABA behavioral research design, compared efficacy of dietary management, hetero- and autohypnotic procedures, wrist band (pain) aversion, and olfactory aversion/covert sensitization procedures.

Results to Date:
The utility of dietary management, hypnobehavioral procedures, and pain aversion was not demonstrated. However, results of olfactory aversion employing valeric acid paired with distasteful covert sensitization suggestions achieved cessation of tobacco use on the first day of treatment. Abstinence was maintained during 5-month followup.

Future Plans:
Olfactory aversion/covert sensitization procedure will be tailored and focused on smoking cessation in an expanded multitreatment group design.

Project Dates:
May 1982–January 1983.

Colorado

0750. COLORADO STATE UNIVERSITY, Department of Zoology, Fort Collins, Colorado 80523.

Project Title:
Interrelationships of Smoking and the Aging Process.

Principal Investigator:
Wilber, C.G.

Objective:
To determine whether there is an interaction between smoking and the aging process in humans.

Methods or Approach:
Information published in conventional literature and in "documents" literature is studied and evaluated. Various demographic sources are also used. Models that may tie together various data on smoking and aging are tested to ascertain whether rational relationships can be shown.

Results to Date:
There are indications that in certain specific aspects, the relationship between aging and smoking may be different in men compared with women. The aging-menopause-smoking troika in women suggests adverse effects are magnified in females. The adverse effects of passive smoking, although apparently real, raise further questions, since older literature does not indicate such harm. However, it may not have been recognized, current tobacco may be different, or smoking practices may have changed.

Project Dates:
September 1974–continuing.

Financial Support:
Colorado State University.

0751. COLORADO STATE UNIVERSITY, Department of Zoology, Fort Collins, Colorado 80523.

Project Title:
Biological Implications of Trace Elements, Especially Selenium, in Tobacco and Its Smoke.

Principal Investigator:
Wilber, C.G.

Objective:
To ascertain what effects, if any, selenium and other trace elements may have on persons who used tobacco or its products.

Methods or Approach:
Pertinent literature is reviewed, and in connection with ongoing selenium studies and beryllium research, an attempt is made to use "materials of opportunity" to expand data on trace elements in tobacco with reference to potential biological effects.

Results to Date:
Selenium is present in tobacco and in some cigarette papers. The potential of selenium content of tissues as a useful test for cancer is suggested but not proved. Interaction of compounds such as selenium-beryllium-cadmium in tobacco might be a productive area of investigation.

Project Dates:
September 1975–continuing.

Financial Support:
Colorado State University.

0752. NATIONAL CENTER FOR ATMOSPHERIC RESEARCH, 1850 Table Mesa Drive, P.O. Box 3000, Boulder, Colorado 80307.

Project Title:
Synergistic Interactions of Indoor Radon Progeny and Cigarette Smoke.

Principal Investigator:
Martell, E.A.

Objective:
To determine properties of radon decay products associated with cigarette smoke particles in smoke-filled rooms and in mainstream cigarette smoke, particularly size distributions, solubility, and other properties that influence deposition and clearance in bronchi of smokers.

Methods or Approach:
Cigarette smoke particles in experimental chambers and in mainstream smoke are tagged with 10.6 hour ^{212}Pb, a convenient radioactive tracer. Size distributions are determined using multistage cascade impactors and low-level β counting methods.

Results to Date:
Radon decay products are concentrated on smoke tar particles of 1 to 2 μm diameter and larger. The larger radioactive particles and dense mainstream smoke column behavior give rise to very selective deposition in "hot spots" at bronchial bifurcations. The relatively slow rate of dissolution of smoke

tars in lung fluid indicates substantial radioactive decay at deposition sites before clearance.

Future Plans:

It is anticipated that deposition patterns for ^{212}Pb-tagged mainstream smoke in hollow casts of the upper bronchial tree will be evaluated experimentally.

Project Dates:

July 1980–October 1985.

Financial Support:

NCAR; NSF; EPA Office of Radiation Programs (AD-49-F-0-78-0).

References:

(1) Martell, E.A.; Sweder, K.S. "The Roles of Polonium Isotopes in the Etiology of Lung Cancer in Cigarette Smokers and Uranium Miners." In: Gomez, M. (Editor). *Radiation Hazards in Mining.* New York, A.I.M.E., 1981, Chapter 61.
(2) Martell, E.A. "α-Radiation Dose at Bronchial Bifurcations of Smokers From Indoor Exposure to Radon Progeny." *Proceedings of the National Academy of Science USA (Biophysics)* 80:1285-1289. March 1983.

0753. NATIONAL JEWISH HOSPITAL AND RESEARCH CENTER, 3800 East Colfax Avenue, Denver, Colorado 80206.

Project Title:

Pathogenesis of Inflammatory Lung Injury.

Principal Investigator:

Henson, P.M.

Objective:

To study the mechanisms of induction of acute inflammatory lung injury and the progression toward chronic disease.

Methods or Approach:

In experimental animals (rabbits and mice), the basic mechanisms of inflammation are being pursued. No specific model of the human disease has been established, rather models of inflammatory processes are initiated to answer specific questions. The role of C5 (fifth component of complement) in initiating the influx of inflammatory cells and thus the acute tissue injury is a specific focus. The mechanisms by which leukocytes migrate out of the blood vessel through the alveolar wall and into the alveolar air space are being studied morphometrically in vivo and by establishing models of blood vessel walls in vitro. The site of C5 synthesis in the lung is studied by examining isolated cells in tissue culture or reinstillation of cells into congenic C5-deficient mice. The controlling processes (inhibitors) which limit the extent of the inflammation induced by C5 fragments or C5 cleavage are being examined by purification of the inhibitors and their later reinstillation into the lung.

Results to Date:

Results indicate that the C5a "des Arg" form is the potent C5 fragment in pulmonary inflammation in the rabbit. C5a, the parent molecule, is relatively inactive but is rapidly converted by carboxypeptidase (which is present in the lung) to the "des Arg" form. C5 is present in the lung, apparently at higher relative concentrations than in the plasma, implying local synthesis. Finally, instillation of immune complexes into mice genetically deficient in C5 results in minimal inflammation by comparison with the effect in C5-sufficient congenic controls. On the other hand, activation of complement intravascularly or instillation of C5 fragments intravenously results in pulmonary sequestration of leukocytes, but no transvascular migration. Therefore, a secondary attractive stimulus (chemoattractant) is necessary for pulmonary inflammation to occur. One source of such chemoattractants is the alveolar macrophage, which has been shown to synthesize and secrete a 10,000 molecular weight chemoattractant for neutrophils upon stimulation by uptake of particles, phospholipase A_2, or arachidonic acid. The possibility that engulfment of membranes and/or surfactant by alveolar macrophages would stimulate the release of such chemoattractants as well as other phlogistic constituents from macrophages is of interest.

Future Plans:

The cells that synthesize C5 (probably macrophages) will be studied. The role of C5 in initiating inflammation by nonimmunologic stimuli including hyperoxia and exposure to tobacco smoke in the congenic mouse strains will also be pursued. The role that neutrophils play in attracting mononuclear phagocytes into the lung, the neutrophil-derived chemoattractant for monocytes, and the effect of this chemoattractant on monocyte differentiation will be examined. Inhibitors of complement activation, as well as of neutrophil secretion, will be isolated from the lavage fluids of normal rabbits and rabbits with inflammation to determine their mode of action and possible therapeutic implications.

Project Dates:

February 1975–continuing.

Financial Support:

NHLBI (HL-21565).

0754. UNIVERSITY OF COLORADO, INSTITUTE FOR BEHAVIORAL GENETICS, Boulder, Colorado 80309.

Project Title:

Heredity and Environment in Drug Use: Separated Twins.

Principal Investigator:

Plomin, R.

Objective:

To study the etiology of drug use in a large sample of middle-aged, same sexed twins reared apart from early childhood and a matched control sample of twins reared together.

Methods or Approach:

The twins have been identified in the Finnish Twin Registry. A questionnaire concerning use of common drugs, such as tobacco, alcohol, tranquilizers, and sleeping pills, will be constructed and sent to the twins. Analyses will focus on the estimation of hereditary as well as environmental influences on the use of these drugs. A major set of analyses will consider the etiology of polydrug use through estimates of "genetic correlations" and "environmental correlations." In addition, the design will permit analyses of (1) the effect of age of separation of twins in smoking and nonsmoking families in order to assess the influence of early "passive smoke" on later tobacco use; (2) the effect of age of separation of the twins in order to assess the influence of early rearing similarity on later similarity in drug use; (3) the interaction between the etiology of drug use and age; (4) the interaction between the etiology of drug use and gender; (5) the extent to which etiological factors involved in extreme drug use are similar to those involved in less extreme drug use; and (6) genotype–environment interaction.

Results to Date:

Although the project was terminated in 1981, an extensive polydrug use questionnaire was developed for use with older individuals. In addition, some analyses were conducted for elderly separated twins in Sweden; over 200 pairs of twins separated in childhood and at the time of testing about 55 years old. Correlations were about 0.25 for twins reared apart for smoking, alcohol use, heavy drinking, caffeine use, and use of sleeping pills. Age at separation does not affect correlations, indicating that early environment is not an important factor in later drug use. Results were compared with matched twins reared together and findings were confirmed, with the added suggestion of some role for shared family environment in the use of common drugs.

Project Dates:
May 1980–1982.

Financial Support:
NIDA (R01 DA02613-02).

0755. UNIVERSITY OF COLORADO, HEALTH SCIENCES CENTER, 4200 East Ninth Avenue, Denver, Colorado 80262.

Project Title:
Maternal O_2 Transport During Pregnancy at High Altitude.

Principal Investigator:
Moore, L.G.

Objective:
To determine how well and by what mechanisms arterial oxygenation was maintained during pregnancy at high altitude; and if variation in maternal characteristics acting to lower arterial oxygenation (including smoking) would contribute to lower infant birth weight and increased maternal and neonatal complications at high altitude.

Methods or Approach:
Measurements of maternal arterial oxygenation at high altitude (3100 m)–ventilation, blood O_2 and CO_2 tensions and pH, hemoglobin concentration, and hemoglobin-O_2 affinity–were made in 44 women using conventional physiological techniques. The same measurements plus assessments of ventilatory sensitivity to hypoxia and hypercapnia are currently being made at low altitude (1600 m) in 22 women in Colorado. Women are studied serially during pregnancy (weeks 20, 30, and 36) and at 3 months postpartum for a measurement in the nonpregnant state. Women who smoke during pregnancy are distinguished from nonsmokers by history and by measuring carboxyhemoglobin level. Information on pregnancy outcome (including infant birth weight, gestational age, neonatal and maternal complications) is collected for each subject.

Results to Date:
Hyperventilation and higher hemoglobin levels maintain arterial oxygenation during pregnancy at 3100 m at levels comparable to published sea level values. At 3100 m, mothers of smaller babies (less than 2900 g) compared to mothers of larger babies (greater than 3500 g) hypoventilate and have a fall in arterial O_2 saturation and hemoglobin concentration from early to late gestation and, hence, have lower levels of arterial oxygenation. Women who smoke during pregnancy at 3100 m have full-term babies which, on the average, are 5-6 g smaller than full-term babies born to nonsmoking mothers at 3100 m. Pregnancy-induced hypertension is more common at 3100 m than at 1600 m.

Future Plans:
Future studies will be concerned with the mechanisms by which pregnancy influences maternal ventilation and will not specifically address the effects of smoking.

Project Dates:
July 1978–continuing.

Financial Support:
NHLBI (HL-14985); American and Colorado Health Associations (80-837); March of Dimes (6-169).

0756. UNIVERSITY OF COLORADO, SCHOOL OF DENTISTRY, 4200 East Ninth Avenue, Box C285, Denver, Colorado 80262.

Project Title:
Oral Tissue Alterations Associated With the Use of Smokeless Tobacco by Teenagers.

Principal Investigators:
Greer, R.O., Jr.; Poulson, T.C.

Objective:
To determine the prevalence and frequency of oral hard- and soft-tissue alterations associated with the use of smokeless tobacco in a teenage population.

Methods or Approach:
High school students in grades 9 to 12 were evaluated on a random basis. From a total sample of 1,119 students, 117 users of smokeless tobacco were identified. Four distinct lesions clinically associated with smokeless tobacco use were (1) hyperkeratotic or erythroplakic lesions of the oral mucosa; (2) gingival or periodontal inflammation; (3) a combination of oral mucosal lesions and periodontal inflammation; and (4) cervical erosion of the teeth.

Results to Date:
Among the users (113 boys and 4 girls), 48.7 percent had soft-tissue lesions and/or periodontal inflammation or erosion of dental hard tissues. Smokeless tobacco use ranged from 1 to 20 "dips"/day, with an average time per dip of 30 minutes. Most users had been dipping for an average of 2 years. Twelve different tobacco brands were identified.

Financial Support:
NIH (DE-06313, CA-21098); ACS; Sands House Association.

0757. UNIVERSITY OF COLORADO, INSTITUTE FOR BEHAVIORAL GENETICS, Box 447, Boulder, Colorado 80309.

Project Title:
Genetics of Nicotine Tolerance: Role of Receptors.

Principal Investigator:
Collins, A.C.

Objective:
To assess the potential function of brain nicotinic receptors in behavioral and physiological responses to nicotine; determine the role of genetic factors in regulating nicotine response and receptors.

Methods or Approach:
Inbred strains of mice are being screened for differences in acute response to nicotine or in development of tolerance to nicotine following chronic intravenous infusion. A battery of measures of behavioral and physiological responses has been developed to assess effects. Measures are being correlated with measures of brain nicotinic receptors obtained using radiolabeled nicotine and α-bungarotoxin as ligands.

Results to Date:
Among strain differences detected, the most interesting is that C3H mice are extremely sensitive to nicotine-induced seizures, while DBA mice are relatively resistant. Segregation analysis suggests that nicotine-induced seizures may be controlled by a single gene that demonstrates dominance toward the DBA-like form. A high correlation between sensitivity to nicotine-induced seizures and the number of hippocampal binding sites has been observed. Strain differences in development of tolerance have also been found, accompanied by an increase in brain nicotinic receptors. The strain that develops the least tolerance (C3H) exhibits only a modest upregulation of brain

nicotinic receptors; other strains that develop considerable tolerance (DBA, C57BL, BALB) exhibit a greater increase.

Future Plans:

Segregation analysis will explore the relationship between tolerance development and receptor changes, and attempts will be made to assess the function of brain nicotinic receptors in regulating neuronal excitability.

Project Dates:

September 1983–September 1986.

Financial Support:

NIDA (5R01DA03194).

0758. UNIVERSITY OF COLORADO, SCHOOL OF MEDICINE, Department of Pediatrics, B 196, Program in Fetal Medicine and Surgery, Denver, Colorado 80262.

Project Title:

Human Placental Metabolism: Responsive Enzyme Systems.

Principal Investigator:

Manchester, D.K.

Objective:

To determine the biologic significance of induction of human placental detoxication systems by exogenous agents such as constituents of cigarette smoke.

Methods or Approach:

Placentas are obtained at birth from normal and abnormal pregnancies and subcellular fractions prepared. Maternal smoking status is determined by history and measurement of cord blood thiocyanate levels. Activities and molecular characteristics of detoxication enzyme systems (cytochrome P-450 monooxygenases, epoxide hydrolases, glutathione S-transferases) are determined and correlated with pregnancy history and outcome. Cells cultured from placenta, membranes, and other products of conception are exposed to inducing agents in vitro and inducibility (i.e., ratio of treated to nontreated enzyme activities) is determined, which are correlated pregnancy history and outcome.

Results to Date:

The human placental aryl hydrocarbon hydroxylase system, which is increased following maternal exposure to smoke, is similar to the system responding to polycyclic aromatic hydrocarbon exposures in mice. Activity of human placental aryl hydrocarbon hydroxylase systems reflects both genetic and environmental input. Lack of activity induction correlates with presence of major congenital anomalies in offspring of women who smoke. Maternal cigarette smoking also induces metabolism of benzo(*a*)pyrene in trophoblastic, but not umbilical vein endothelial tissue in vivo. Umbilical vein endothelium, however, is inducible in vitro. Results may indicate a protective effect of placental xenobiotic metabolism.

Future Plans:

Projects will seek to characterize the nature of genetic control of placental xenobiotic metabolism and to determine whether the resulting phenotypes affect risks for maldevelopment.

Project Dates:

July 1978–continuing.

Financial Support:

NICHD (R01HD12936); University of Colorado School of Medicine; Colorado Medical Services Foundation, National Foundation, March of Dimes.

0759. UNIVERSITY OF COLORADO, Box C322, 4200 East Ninth Avenue, Denver, Colorado 80262.

Project Title:

Role of RBC Antioxidants in Cigarette Smoke Related Diseases.

Principal Investigators:

Repine, J.E.; Berger, E.M.; Beehler, C.J., et al.

Objective:

To determine if variations in red blood cell (RBC) antioxidants affect and/or predict susceptibility to oxidant induced lung and/or cardiovascular or malignant disorders.

Methods or Approach:

RBCs are obtained from human cigarette smokers or animals exposed to smoke. Antioxidant capabilities are tested in vitro (endothelial cell culture and isolated perfused lungs exposed to O_2 metabolites from phagocytes or chemical generators).

Results to Date:

RBCs from cigarette smokers contain more glutathione and catalase and protect lung endothelial cells against O_2 metabolites better than RBCs from nonsmokers.

Future Plans:

Research will seek to further define basic mechanisms by which exposure to cigarette smoke alters RBC antioxidant enzymes and the significance of the changes.

Project Dates:

January 1980–continuing.

0760. UNIVERSITY OF COLORADO, SCHOOL OF PHARMACY, Boulder, Colorado 80309.

Project Title:

Chromatographic Separation and Comparative Metabolism of d- and l-Nicotine.

Principal Investigator:

Thompson, J.A.

Objective:

To (1) develop chromatographic methods to separate and quantitiate d- and l-nicotine at nanogram levels in biological samples; (2) measure degree of racemization of l-nicotine in burning tobacco by quantitating d-nicotine in tobacco smoke and in smoke-exposed rats and mice; and (3) investigate effects of sterochemistry on metabolism and disposition of d- and l-nicotine in rats and mice.

Methods or Approach:

Stereoisomers of nicotine will be separated by converting nicotine to nornicotine by chemical methods and derivatizing nornicotine with various chiral reagents. Resulting diastereomeric derivatives will be separated by gas chromatography and high performance liquid chromatography. Nicotine will be trapped from tobacco smoke and isomer composition determined as described. Pharmacokinetic and metabolic profiles of nicotine will be determined by injecting rats and mice with d- or l-nicotine and with racemic nicotine to determine effects of stereochemistry on nicotine disposition.

Results to Date:

Methods have been developed to convert nicotine to nornicotine and, subsequently, to diastereomeric derivatives. Derivatives formed with (R)-naphthyl ethylisocyanate and an optically pure peracetylated derivative of β-D-glucopyranosyl isothiocyanate can be resolved chromatographically. Methods are being applied to determination of nicotine racemization in tobacco smoke and to effects of stereochemistry on nicotine pharmacokinetics and metabolism in rats and mice.

Project Dates:

July 1983–June 1986.

Financial Support:
CTR (1575).

0761. UNIVERSITY OF COLORADO, HEALTH SCIENCES CENTER, Department of Family Medicine, 1180 Clermont Street, Denver, Colorado 80220.

Project Title:
Health Promotion/Disease Prevention: Residency Training Program in Family Medicine.

Principal Investigators:
Chu, F.; Lewis, B.

Objective:
To (1) develop and implement a curriculum designed to teach family medicine residents the knowledge base, skills, and attitudes needed to reduce health risks in patients; (2) develop model health promotion services demonstrating use of allied health professionals and successful patient teaching methods and techniques that are applicable to future family medicine practice settings; (3) teach residents how to counsel patients on smoking cessation, including use of nicotine chewing gum; and (4) instruct residents on the risk of smoking and how it interacts with other risk factors.

Methods or Approach:
The curriculum consists of (1) one-on-one precepting of all residents by a health educator who interacts with patients on health promotion issues, including smoking and smoking cessation; (2) conferences (similar to grand rounds); (3) modules that contain brief protocols and other pertinent information, including a smoking protocol (written at Mercy Medical Center) that is being pilot tested; (4) patient education materials; and (5) intensive training for first year residents (approximately 25 hours).

Results to Date:
During the first year, 24 residents were precepted an average of four times; 12 hours of conferences were held, including 2 hours on smoking and use of nicotine gum and 3 hours on smoking for first year residents. There were numerous consultation requests, primarily for smoking cessation. Significant quantities of educational materials were distributed to patients. Results of content evaluation are not yet available.

Future Plans:
Plans are to teach residents in family medicine (and possibly internal medicine) by offering intensive workshops and possibly personal consultation.

Project Dates:
July 1984–June 1986.

Financial Support:
PHS.

0762. UNIVERSITY OF COLORADO, HEALTH SCIENCES CENTER, Denver, Colorado 80262.

Project Title:
Smoking, Weight Gain, and Lipoprotein Lipase.

Principal Investigators:
Eckel, R.H.; Sadur, C.N.; Yost, T.J.

Objective:
To determine the relationship between activity of the adipose-tissue enzyme and changes in body weight in adult smokers.

Methods or Approach:
After measurement of lipoprotein lipase activity in gluteal adipose tissue in overweight fasting adults, 8 smokers and 22 nonsmokers were placed on hypocaloric diets. Smokers were defined as persons who smoked > 10 cigarettes/day.

Results to Date:
Lipoprotein lipase activity was similar in smokers and nonsmokers. When lipoprotein lipase activity was expressed as nanoequivalents of FFA/min/g tissue, a similar relationship between smokers and nonsmokers was found (not significant). All but two patients ingested very-low-protein liquid diets and caloric intake in all was restricted to between 325 and 675 kcal/day. After 3 weeks of dieting, there was no relationship in nonsmokers between the amount of weight change and lipoprotein lipase activity. However, in smokers the amount of weight change was related to the previously determined activity of lipoprotein lipase in adipose tissue; overweight smokers with higher activities of lipoprotein lipase in adipose tissue lost less weight than those with lower enzyme activity. Thus, activity of lipoprotein lipase in gluteal adipose tissue is predictive of short-term weight gain in former smokers and of short-term weight loss in dieting smokers. The failure of the adipose-tissue enzyme activity to predict weight loss in nonsmoking dieters suggests a smoking-dependent alteration in energy conservation of caloric intake. The mechanism of such an effect remains to be clarified.

Project Dates:
December 1979–continuing.

Financial Support:
University of Colorado; NIH (AM 26356); Cambridge Quest Foundation.

Reference:
Eckel, R.H.; Sadur, C.N.; Yost, T.J. "Smoking, Weight Change, and Lipoprotein Lipase." *New England Journal of Medicine* 311(4):259-260, July 26, 1984.

0763. UNIVERSITY OF COLORADO, SCHOOL OF PHARMACY, Campus Box 297, Boulder, Colorado 80309.

Project Title:
Effects of Nicotine on Neuropeptide Secretion by Intact Mouse Brain; A Pharmacogenetic Study.

Principal Investigators:
Erwin, V.G.; Marty, M.A.

Objective:
To determine effects of nicotine on levels of somatostatin, bombesin, β-endorphin, met-enkephalin, and ACTH in various regions of isolated perfused mouse brains (IPMB) from C3H and DBA inbred strains of mice; determine effects of nicotine on release and secretion of somatostatin, bombesin, β-endorphin, met-enkaphalin, and ACTH.

Methods or Approach:
Studies are conducted by trained personnel with expertise and competence in high performance liquid chromatography (HPLC) systems, isolated brain perfusions, and radioimmunoassays (RIA). Experiments involve brain perfusions and pituitary superfusions, coupled with HPLC and RIA analysis of catecholamine metabolites and neuropeptides.

Results to Date:
C3H mice are behaviorally activated by doses of ≤ 1 mg/kg of nicotine while C57BL mice are behaviorally sedated. The strains also differ on effects on body temperature. Using mouse brains from both strains, it was shown that nicotine elicits a differential effect on neuropeptide secretion and on catecholamine metabolism. While nicotine stimulates release of β-endorphin, ACTH, and α-MSH from the pituitary via a centrally mediated mechanism, some of the behavioral effects of nicotine are apparently not mediated by this effect. For example, dexamethasone (POMC release blocker) did not alter nicotine-induced open-field activation or depression in C3H

and C57BL mice, respectively; however, it did block or reverse nicotine-induced hypothermia in both strains, implicating a role of POMC peptides in some of the effects of nicotine.

Project Dates:
July 1982–June 1985.

Financial Support:
CTR.

0764. VETERANS ADMINISTRATION MEDICAL CENTER, 2121 North Avenue, Grand Junction, Colorado 81501.

Project Title:
Lung Study of High Risk Population.

Principal Investigator:
Saccomanno, G.

Objective:
To conduct sputum studies of high-risk patients.

Methods or Approach:
A sputum study was begun in October 1980 of high-risk patients admitted to the VA Medical Center, Grand Junction, Colorado, who were not admitted for treatment of lung cancer. Patients on whom sputum studies are performed must be over 40 years of age and must be cigarette smokers.

Results to Date:
Of the 1,551 cases studied between October 1980 and July 1984, 739 had mild atypia, 136 had moderate atypia, 16 had marked atypia, and 15 (including 5 miners) were suspicious for malignancy. Positive sputum evidence of malignancy was found in 33 cases (12 cases were miners). Analysis indicates studies are worth performing. Data collection will be continued for another year to establish more valid statistical data.

Financial Support:
VA.

Connecticut

0765. HARTFORD HOSPITAL, Hartford, Connecticut 06115.

Project Title:
Correlation of Risk Factors for Arterial Disease and Penile Brachial Index (PBI) in Erectile Dysfunction.

Principal Investigator:
Wabrek, A.J.

Objective:
To determine if low penile systolic blood pressure or PBI is correlated with other manifestations of arterial disease.

Methods or Approach:
In a group of males with erectile dysfunction, sexual history will be recorded and noninvasive penile arterial assessment will be made. Questionnaires will provide data on other risk factors for arterial disease.

Results to Date:
Results are not yet available.

Project Dates:
1983–1986.

0766. JOHN B. PIERCE FOUNDATION LABORATORY, 290 Congress Avenue, New Haven, Connecticut 06519.

Project Title:
Perceived Intensity of Odorants and Irritants.

Principal Investigator:
Cain, W.S.

Objective:
To (1) investigate the chemosensory impact of airborne agents, particularly those with irritating capability, on human subjects; (2) determine threshold of irritation, perceived magnitude of irritation over time; (3) study the tendency of exposure to an irritant to produce decrements in chemosensory functioning; and (4) develop objective tests for chemosensory functioning.

Methods or Approach:
Agents studied include tobacco smoke, formaldehyde, and ammonia. Methods include standard techniques of psychophysics (threshold techniques, scaling techniques) and measurement of nasal resistance, reaction time, breathing patterns, and transitory apnea upon irritant stimulation.

Results to Date:
Recent findings include (1) smokers are less sensitive to nasal irritation than nonsmokers; (2) using short-term stimulation, the pungency of ammonia to the nose may produce constant perceived intensity in time; (3) formaldehyde also causes increasing intensity with time and affects the eyes, nose, and throat about equally; (4) elderly people (nonsmokers) have impaired ability to perceive odors and irritants; and (5) a measure of reflex apnea in response to irritant stimulation gives a realistic objective picture of the sensitivity of the irritant sense.

Project Dates:
May 1982–May 1986.

Financial Support:
NIEHS (ES00592).

0767. VETERANS ADMINISTRATION MEDICAL CENTER, SCHOOL OF MEDICINE, Building 5, Newington, Connecticut 06117.

Project Title:
Cholinergic/β-Endorphinergic Reinforcement of Smoking.

Principal Investigator:
Pomerleau, O.F.

Objective:
To integrate the behavioral (psychological) research on nicotine and smoking with biochemical (neuroendocrinological and pharmacological) investigations of neuropeptide activity at the normal human level; demonstrate, using behavioral markers and biochemical measurements, the contribution of one neuropeptide, β-endorphin, to the reinforcement of smoking.

Methods or Approach:
A repeated-measures within subjects design is used, with different experimental conditions studied over successive days and simultaneous measurement of subjective, behavioral, physiological, and biochemical variables. Specifically, the research should (1) demonstrate the effects of nicotine intake from smoking on relevant behavioral markers of cholinergic/β-endorphinergic activity (cold-water pain and puzzle anxiety); (2) determine whether pain reduction (antinociception) from smoking is due to the termination of nicotine withdrawal or to nicotine effects independent of withdrawal; (3) establish

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whether the frequency or intensity of smoking is increased by a dysphoric state not associated with the nicotine addiction cycle, such as anxiety; and (4) sort out the relative contribution of nicotinic cholinergic activity and β-endorphinergic activity on pain and anxiety responses through the administration of a cholinergic blocker (mecamylamine), an opiate antagonist (naloxone), or synthetic β-endorphin. The health implications are that a better understanding of underlying biobehavioral mechanisms in smoking and substance abuse may make possible the development of rational therapies of greater effectiveness than are currently available.

Results to Date:
Project is in a preliminary phase.

Project Dates:
April 1984–March 1987.

Financial Support:
NCI (1R01CA38087-01).

0768. VETERANS ADMINISTRATION MEDICAL CENTER, West Spring Street, West Haven, Connecticut 06516.

Project Title:
Bronchoalveolar Lavage Fluid in Pulmonary Carcinoma - Secretory Component of Immunoglobulin A as A Marker of Neoplastic Growth.

Principal Investigators:
Reynolds. H.Y.; Merrill, W.W.; D'Esopo, N.

Objective:
To assess (by chest radiograph) the quantity of secretory component (SC) in lower lung airway secretions as an indicator of ciliated epithelial dysfunction in patients at high risk to develop lung cancer (cigarette smokers) or in those who have already developed a lung mass.

Methods or Approach:
The SC glycoprotein molecule, synthesized and secreted by the epithelial cell, subsequently couples with secretory IgA immunoglobulin. Since there is no effective cure for lung cancer even with optimal surgical extirpation, emphasis must be on early detection of cellular biochemical changes in susceptible people (i.e., epithelial secretion in cigarette smokers) before cytological atypia develops. Currently, lung secretions are obtained by lung lavage (BAL) during diagnostic fiberoptic bronchoscopy in patients with a potentially resectable lung mass. The study is being conducted at the West Haven VA and Yale New Haven Hospitals.

Results to Date:
In the past year, 11 patients participated (2 at West Haven); since initiation of the study (1977), 120 patients have participated (44 were patients at West Haven). No significant complications have occurred. Results show (1) heavy cigarette smokers have lower SC values (calculated as percent of total BAL protein) than light smokers (<10 pack-years) or nonsmokers; (2) smoking patients with histologically proven squamous cell carcinoma have very low, often undetectable, SC values; and (3) patients with other tumors (adenocarcinoma or oat cell) have intermediate SC values that probably reflect smoking history. It appears that smoking and presence of a squamous cell tumor will correlate with diminished SC, suggesting secretory dysfunction of lung epithelium. Carcinoembryonic antigen (CEA) is also increased in BAL from patients. Preliminary results of CEA in normal controls have been reported.

Financial Support:
VA.

References:
Merrill, W.W.; Goodman, M.; Matthay, R.A., et al. "Quantitation of Carcinoembryonic Antigen in the Lung Lining Fluid of Normal Smokers and Nonsmokers." *American Review of Respiratory Disease* 123:29-31, January 1981.

0769. VETERANS ADMINISTRATION, West Spring Street, West Haven, Connecticut 06516.

Project Title:
Respiratory Tract Glycoproteins as Markers of Inhalant Induced Lung Disease.

Principal Investigators:
Merrill, W.W.; Reynolds, H.Y.

Objective:
To develop markers in subjects susceptible to smoking-related respiratory disease prior to the development of symptomatic disease.

Methods or Approach:
Respiratory tract fluid will be obtained from nasal washings, bronchial lavage, and parotid fluid from four groups (young nonsmokers, young healthy smokers, patients with pulmonary carcinoma, and patients with carcinoma of the upper respiratory tract). Fluids from a subgroup of young smokers will be studied in the hope of detecting alterations in certain respiratory tract proteins that are similar to alterations seen in diseased patients. Fluids will be analyzed using a variety of biochemical and immunochemical techniques. Proteins to be analyzed include free secretory component, a glycoprotein synthesized by bronchial mucosal cells (thus a marker of cell health), and carcinoembryonic antigen, a protein present in increased concentration in neoplastic tissues.

Results to Date:
The last year has been spent developing a new immunoassay for free secretory component.

Financial Support:
VA.

0770. YALE UNIVERSITY SCHOOL OF MEDICINE, Department of Epidemiology and Public Health, Connecticut Cancer Epidemiology Unit, 60 College Street, New Haven, Connecticut 06510.

Project Title:
Development of a Database in the Connecticut Tumor Registry (CTR) for Including Current Occupation/Industry and Smoking Status of Cancer Patients and Study of Factors Influencing Availability of Data in Patients' Hospital Records.

Principal Investigators:
Curnen, M.G.M.; Thompson, W.D.

Objective:
To (1) search for factors in the medical records of cancer patients that are most likely to contribute to the presence or absence of data on occupation and smoking status; (2) gather information on the time interval that elapsed between the date of diagnosis of cancer in the hospital and notification to the Connecticut Tumor Registry; (3) analyze data to suggest methods for improving the rapid monitoring system of cancer incidence by population-based tumor registries; and (4) facilitate the conduct of case-control studies requiring interviews.

Methods or Approach:
Over 1,550 tumor records at the CTR were reviewed for factors likely to determine whether data on occupation/industry and smoking were collected and included in patient's paper records (routinely submitted to the CTR by all 35 hospitals in the State). Random samples from 1981 and

1982 were compared with samples from 1983 for presence or absence of data. The following were recorded and are being analyzed: patient's sex, age, race, site of cancer, date of admission, and characteristics of admitting hospital. Standardized data on occupation/industry and smoking, to be collected on all inpatients, will provide means for comparing occupational hazards in cancer patients with those in patients hospitalized for other conditions. For cancer patients, data will provide the basis for developing and maintaining information necessary for an ongoing registry of exposure to smoking and other environmental hazards (a valuable addition to the population-based CTR).

Results to Date:
Final results are not yet available, but interim reports, listed below, have been published.

Project Dates:
1983–1985.

Financial Support:
Yale University School of Medicine; NCI (N01CP33235/No 1 CN 33235; N01CP61002; CA 16359).

References:
(1) Curnen, M.G.M.; Schoenfeld, E.R. "Standard Information of Environmental Exposure Linked to Data on Cancer Patients, With a Brief Review of the Literature." *Preventive Medicine* 12:242-261, 1983; (2) Curnen, M.G.M.; Thompson, T.W.; Heston, J.F., et al. "Cancer Prevention: The Tumor Registry Connection." *Cancer Detection and Prevention* 7:191-199, 1984; (3) Curnen, M.G.M. "Lung Cancer in Connecticut Women." *Lancet* 2:906-907, 1983.

0771. YALE UNIVERSITY SCHOOL OF NURSING, 813 Orange Street, New Haven, Connecticut 06511.

Project Title:
Cigarette Smoking: Nurse Practitioners' Knowledge, Attitudes, and Role in Intervention. (Master's Thesis).

Principal Investigator:
McNelly, E.A.

Objective:
To (1) examine nurse practitioners' knowledge, attitudes, and clinical practice related to cigarette smoking; (2) establish relationships between these and various demographic variables; and (3) identify factors associated with a greater likelihood of practitioner involvement in antismoking activities.

Methods or Approach:
A self-administered, researcher-designed questionnaire was mailed to a convenience ample of 450 nurse practitioners (NPs) living in the northeastern United States. Questions covered demographics, practice, attitudes, and knowledge about cigarette smoking and included items developed and utilized by the U.S. Department of Health, Education, and Welfare and the Connecticut American Cancer Society Nursing Committee to facilitate cross-comparison of studies. Computer analysis was performed using standard statistical techniques.

Results to Date:
The nurses who responded (n=252, 56 percent) were better informed than health professionals in previous surveys. The sample subjects also felt highly obligated to be involved in a number of antismoking roles and were optimistic about nurses' potential impact on smoking-related health problems. Thesis includes data on smoking cessation strategies used by NPs in practice, frequency with which a given method was perceived as helpful, and client, setting, and NP characteristics felt to influence the decision to intervene. A number of small but significant relationships were found among subject's knowledge, attitudes, and practice scale scores and demographic variables. Only 14 percent of the NPs were current smokers. Implications for clinical practice are also discussed, including the need for increased attention to ex-smokers and nonsmokers.

Future Plans:
Data analysis will be completed and results will be published.

Project Dates:
January 1983–May 1984.

Financial Support:
Yale University of Nursing; ACS.

0772. YALE UNIVERSITY, SCHOOL OF MEDICINE, 333 Cedar Street, New Haven, Connecticut 06510.

Project Title:
Pregnancy Complications After Induced Abortion.

Principal Investigators:
Bracken, M.B.; Warshaw, J.E.; Hobbins, J.C., et al.

Objective:
To estimate the relative and attributable risks of different induced abortion experiences and procedures for a number of complications of subsequent pregnancies, labor, deliveries, and newborns.

Methods or Approach:
All women (estimated n=5,000) who have made a first prenatal visit to physicians, health plans and clinics, and who anticipate delivery at Yale-New Haven Hospital, will be invited to participate in the study. To ascertain information about abortion experiences and other risk factors patients will be interviewed, with their physicians' consent, using a standardized questionnaire given by trained interviewers. Supplemental information will be obtained from physicians and clinics where abortion was obtained. Information about pregnancy outcomes will be obtained by surveying all deliveries at the hospital and linking these to respondents who have been interviewed. Obstetricians and patients may be recontacted if necessary. In the analysis, complications of pregnancy, labor, delivery and in newborns will be compared in women exposed and not exposed to prior abortion. Experience of abortion will include number and sequence of abortions, technique used, and gestational age at abortion. Possible confounding factors will be accounted for such as maternal age, pregnancy history, smoking history, history of venereal infections, interpregnancy intervals, and contraceptive use. A multivariate analysis using log linear models will be used that can identify sub-groups of women who have unusually high or low risk of developing complications if exposed to induced abortion.

Results to Date:
Results are not yet available.

Project Dates:
September 1979–December 1982.

Financial Support:
NICHD.

0773. YALE UNIVERSITY, NEW HAVEN MEDICAL CENTER, Yale Comprehensive Cancer Center, 333 Cedar Street, New Haven, Connecticut 26510.

Project Title:
Smokers, Former Smokers, and Nonsmokers: A Comparative Study of Nurses' Attitudes and Quitting Methods.

Principal Investigators:
Knobf, M.K.T.; Morra, M.E.

Objective:
To (1) establish the percentage of nurses presently smoking in Connecticut; (2) pinpoint differences among smokers, former

smokers, and nonsmokers; and (3) identify why quit-smoking clinics did not attract nurses.

Methods or Approach:

A questionnaire based on information generated by a Center for Disease Control survey was sent to 1,119 licensed registered nurses in Connecticut (3 percent random sample). Data were analyzed from completed questionnaires using SPSS statistical package with chi-square tests performed on distributions of subjects by three groups.

Results to Date:

It was found that (1) the percentage of nurses in Connecticut currently smoking has dropped significantly over the past several years and is now less than that of women in the general population (25.5 percent vs. 29.2 percent); (2) there are significantly more nurses aged 45 to 54 who smoke; (3) there are more nurses with bachelor's degrees who have never smoked, and more diploma-prepared nurses who have quit smoking than expected; (4) there are significantly more nurse smokers who have smoked for more than 20 years than former nurse smokers for the same period; (5) cold turkey is the technique used by more than 90 percent of smokers and former smokers; (6) reasons offered by those who failed include loss of determination, stress, weight gain, hyperactivity, and the influence of environments predominated by smokers; (7) the nurse smoker does not identify herself as a health educator as frequently as does the former nonsmoking nurse; (8) the perception of the nurse's role as an example is significantly different among the three groups; (9) significantly fewer nurses who smoke agree that nurses should set a good example, should not smoke while on duty, or should not smoke anywhere in public when in uniform; and (10) 65 percent of smoking nurses report consuming more than 1.5 packs a day, and report smoking more at work than elsewhere.

Project Dates:

September 1979–1982.

Financial Support:

Yale Comprehensive Cancer Center; ACS; NCI (NO-1-CN-55232).

0774. YALE UNIVERSITY, P.O. Box 3333, New Haven, Connecticut 06510.

Project Title:

Environmental Risk Factors Related to Male Subfertility.

Principal Investigator:

Bracken, M.B.

Objective:

To investigate the association between semen abnormalities in an adult male population seeking treatment for subfertility and exposures to environmental agents resulting from occupation and other risk factors associated with personal behavior, including the use of alcohol, cigarettes, drugs, hot baths, and materials related to hobbies.

Methods or Approach:

A case–control study will be conducted among patients seeking treatment at the Yale-New Haven Hospital Infertility Clinic. The male partners of all couples entering the clinic over a 3-year period will be invited to participate, and detailed information will be ascertained concerning (1) medical history, (2) medical therapies, (3) family genetic history, (4) reproductive history, (5) occupational history, (6) military service, (7) recreational activities, and (8) personal habits. Subjects will be physically examined and diagnostic tests, including at least two semen analyses, will be performed. Men with semen abnormalities will be designated as cases and the remaining group will be controls. Data will be analyzed to identify the variables that best differentiate cases from controls, based on various elements in the personal histories. The magnitude of risk for having abnormal semen will be computed for each environmental exposure and for specific types of semen abnormality, for groups of abnormalities, and for all combined. Determination of confounding and effect-modifying factors will be made and controlled for, using log linear models. Final analysis will include multivariate analysis to evaluate risk factor interaction. During the 36 months of recruitment, it is anticipated that 593 cases and 89 controls will be recruited.

Results to Date:

Results are not yet available.

Financial Support:

NICHHD (5R01HD16282-02).

District of Columbia

0775. AMERICAN COUNCIL FOR AN ENERGY-EFFICIENT ECONOMY, 1001 Connecticut Avenue, NW., Suite 535, Washington, D.C. 20036.

Project Title:

Indoor Air Quality and Energy Efficiency.

Principal Investigator:

Morrill, J.H.

Objective:

To (1) identify major indoor air pollutants and their sources and health effects; (2) examine the relationship between indoor air pollutants and energy conservation efforts, particularly in residential settings; and (3) examine techniques for reducing indoor air pollution without compromising energy efficiency.

Methods or Approach:

An extensive literature review will be conducted and communication will be established with indoor air quality researchers and industry associations and representatives. Mathematical modeling of infiltration/ventilation rates and indoor pollution levels will test impact of weatherization and control measures.

Results to Date:

Energy conservation does not cause air pollution, although some energy conservation measures can lead to slightly higher concentrations of some pollutants. However, there are methods currently available that can provide occupants of energy-efficient buildings with much healthier indoor air than that found in many older non-energy-efficient homes. Passive exposure to tobacco smoke is one of the major indoor pollutants of concern. Exposure to smoke is most effectively reduced by reduction in smoking by individuals.

Future Plans:

Plans include publication of consumer and builder guides for reducing exposure to indoor air pollutants without compromising energy efficiency.

Project Dates:

June 1983–September 1985.

Financial Support:

MacArthur Foundation.

0776. ECONOMIC RESEARCH SERVICE, 14th and Independence Avenue, South Building, Washington, D.C. 20250.

Project Title:
Price Relatives, Price Dispersions, and Mark-ups of Processed Food Products.

Principal Investigators:
Connor, J.; Wills, R.

Objective:
To (1) develop 1982 media advertising data to link with new census shipments data and add to 1954, 1967, 1972, 1977 series; (2) measure the informational content of advertising of food; (3) analyze the market structure determinants of variability in food brand advertising intensities; (4) examine impact of the variability in food brand advertising intensities; (5) examine impact of the congressional ban on cigarette advertising on advertising techniques and market shares of tobacco companies; (6) conduct case studies of effects of input procurement practices on finished food product price dispersions; (7) analyze vertical integration, thin markets, and market orders; (8) study influence of industry participation of cooperatives on food pricing behavior; and (9) investigate measurement of undue price enhancement.

Methods or Approach:
Several analyses based on cross-sectional econometric techniques with market structure and control variables will be conducted. Data will be collected at the product class or firm level. Case studies will be based on the historical method.

Results to Date:
Data processing procedures for matching 1982 media advertising expenditures with value of shipment data were developed. Turnover in personnel prevented further progress. The analysis of market structure determinants of variability in food brand advertising intensities was completed and a manuscript reporting the results is in preparation. A manuscript on advertising and promotion in food marketing was completed and is being prepared for publication as a staff report. A price index for cigarette advertising and a market share time series were developed to analyze the effect of a ban on advertising. Case studies of effects of input procurement practices on food product prices were not initiated because of a lack of resources, and the research objectives were incorporated into an FY-1984 project. An analysis of the influence of cooperatives on food pricing behavior and whether or not they contributed to undue price enhancement was completed and a report is being drafted.

Project Dates:
October 1982–September 1983.

Financial Support:
USDA (NED-FMR-4298).

References:
(1) Connor, J.; Ward, R. (Editors). *Advertising and the Food System.* University of Wisconsin, NC-117 Monograph No. 14, November 1982, 490 pp. (2) Connor, J.; Ward, R. "The Regulation of Advertising." *Agricultural Economic Research,* 35(1), 1983.

0777. FEDERAL TRADE COMMISSION, TOBACCO RESEARCH LABORATORY, 6th and Pennsylvania Avenue, NW., Washington, D.C. 20580.

Project Title:
Cigarette Testing.

Principal Investigator:
Pillsbury, H.C.

Objective:
To determine tar, nicotine, and carbon monoxide (CO) content in domestic cigarettes.

Methods or Approach:
In addition to continuing the program of testing and reporting the tar and nicotine content of cigarette smoke, in 1980 the Federal Trade Commission initiated a program to determine and publish CO content. The apparatus to be used incorporated infrared spectrophotometry, an analytical method heretofore not used in the laboratory. CO concentration was to be reported as mg/cigarette.

Results to Date:
The tobacco industry raised objections to the use of the machine, contending that testing for and publication by the Commission would imply, without scientific proof, that CO content has relevance or significance in terms of health. However, after testing, the Commission concluded that it was entirely appropriate to publish a Federal Register notice describing the new smoking machine and the methods to be used by the laboratory for determining CO, tar, and nicotine content of cigarette smoke.

Project Dates:
November 1975–continuing.

Financial Support:
FTC.

0778. GEORGETOWN UNIVERSITY, SCHOOL OF MEDICINE, Department of Anatomy, 3900 Reservoir Road, NW., Washington, D.C. 20007.

Project Title:
Effect of Maternal (Rat) Exposure to Cigarette Smoke on the Cellular and Subcellular Morphometry of the Neonatal Type II Pneumocyte.

Principal Investigator:
Vidic, B.

Objective:
To determine the effect of exposure to whole, high-nicotine (1.91 mg) cigarette smoke of pregnant animals on the prenatal and/or postnatal development sequence of pulmonary cells, in particular the type II pneumocyte.

Methods or Approach:
The sequence was evaluated primarily in relation to subcellular morphometric characteristics (volumetric density of organelles responsible for synthesis, intracellular transport, and secretion of surfactant phospholipids) during early postnatal life. Adult female rats were exposed twice/day for 60 days to smoke from a whole reference cigarette (experimental group), which was administered by the Walton intermittent puff smoking apparatus. The period included premating, mating, and entire pregnancy. Offspring were sacrificed at 4, 13, and 21 days, and lungs were physically evaluated. Pulmonary tissue samples were removed and processed for electron microscopic morphometry. Data on offspring of experimental animals were compared with data from control or sham control animals.

Results to Date:
It was found that the type II pneumocyte was generally larger in experimental group offspring than in controls. In addition, the volume density of lamellar bodies in the cytoplasm and in the whole cell was greater in experimental lungs of all ages compared with control animals. Results suggest that the experimental condition might have a stimulatory effect on prenatal and/or postnatal differentiation of the surfactant phospholipid synthesizing and secreting cell in the lung.

Future Plans:
The same experimental protocol will be applied to new

animals, and cardiopulmonary systems will be used for an in vitro perfusing and ventilation experiment. Results, with morphometric data, will further establish the effect of maternal exposure to whole cigarette smoke on the synthetic and secretory capability for surfactant phospholipids of the type II pneumocyte.

Project Dates:
April 1982–May 1986.

Financial Support:
Georgetown University School of Medicine; NIH.

0779. GEORGETOWN UNIVERSITY, SCHOOL OF MEDICINE, 3900 Reservoir Road, NW., Washington, D.C. 20007.

Project Title:
Abusable Substances, Medicines, and Children Grades K-6.

Principal Investigators:
Bush, P.J.; Davidson, F.R.; Iannotti, R.J., et al.

Objective:
To obtain knowledge directly from children on the development of behaviors, beliefs, and attitudes toward abusable substances and medicine.

Methods or Approach:
This longitudinal study examines developmental precursors in the formation of children's use and expectations to use medicines and abusable substances, primarily cigarettes, alcohol, and marijuana. Three hundred urban children in grades 3 through 7 at schools representing high, medium, and low socioeconomic levels are eligible for reinterview 3 years after initial interview. The children's primary caretakers will also be interviewed. A children's health belief model (CHBM) has been developed, which predicts children's health-related behavior and expectations of health-related behavior. Indices used have been evaluated for internal reliability. The continuation study permits evaluation of (1) the value of family behavior and attitudes in the CHBM; (2) the stability of selected variables in the CHBM over time; (3) the relationship of peers to primary caretakers on selected family influences over time; and (4) the relationship between children and primary caretakers on selected CHBM variables.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Information gained from the study will be useful for health professionals, persons studying children's health beliefs and behaviors, and persons planning and evaluating children's health education and abusable substances intervention programs.

Financial Support:
NIDA (S R01DA2686-04).

0780. GEORGETOWN UNIVERSITY, Department of Community and Family Medicine, Washington, D.C. 20007.

Project Title:
A Replication and Evaluation of the KYB Program.

Principal Investigator:
Bush, P.J.

Objective:
To use a PRECEED model to guide a replication and evaluation of the "Know Your Body" (KYB) program in about 1,500 predominately black urban children in grades 4 through 6, stratified by socioeconomic status.

Methods or Approach:
Lifestyle is believed to account for a considerable proportion of morbidity and premature mortality associated with coronary heart disease (CHD). Many of the behavior patterns associated with risk of cardiovascular disease begin in childhood and are carried into adulthood. Risk factors include smoking cigarettes, obesity, lack of exercise, and a diet high in salt and fats (especially cholesterol). The goal of the KYB program is to reduce children's risk of CHD through a school curriculum that includes personal health screening and addresses children's attitudes and psychosocial moderators as well as knowledge and behavior. Included in the research design is an evaluation of the cost effectiveness of providing personal laboratory and health screening values to each child on a "Health Passport." An effort will be made to reduce the cost of personalized health screening by recruiting and training volunteers. The 5-year project will use the services of health educators, pediatricians, developmental psychologist, medical anthropologist, biostatistician, and medical sociologist.

Results to Date:
Project is in a preliminary phase.

Financial Support:
NHLBI (5R18HL30610-02).

0781. HOWARD UNIVERSITY CANCER CENTER, 2041 Georgia Avenue (Rear), NW., Washington, D.C. 20060.

Project Title:
Hormonal Regulation of Nitrosamine Metabolism.

Principal Investigator:
Mohla, S.

Objective:
To study metabolism of the environmental carcinogen N-nitrodimethylamine, commonly found in cigarette smoke and preserved food; determine its interaction with endogenous sex hormones.

Methods or Approach:
To investigate whether endogenous sex hormones potentiate the carcinogenic effects of N-nitrosodimethylamine (DMN) by stimulating its metabolism to form active metabolites, BALB/c mice are treated with various androgens or androgen-mimicking agents. Microsomes from mouse tissues are used to study in vitro DMS metabolism. DMN-hydroxylase (the enzyme implicated in DMN metabolism) activity is measured colorimetrically by measuring amount of formaldehyde (one of the products of DMN metabolism) formed.

Results to Date:
Although the liver is the primary organ for DMN metabolism, androgen regulation of DMN metabolism occurs only in the kidney of BALB/c mice. Marked sex differences are noted in DMN-hydroxylase activity, with males having higher renal enzyme activity than females. Administration of androgens to adult females increases and orchiectomy of adult male decreases renal DMN-hydroxylase activity. Other androgens, such as methyltrienolone or the androgen-mimicking agent medroxyprogesterone acetate, also stimulate renal DMN metabolism.

Future Plans:
Studies will include (1) metabolism of other nitrosamines and benzopyrenes found in cigarette smoke and their regulation by androgens; (2) DMN metabolism in the lung (the first organ to interact with DMN from cigarette smoke); and (3) effect of other androgens and antiandrogens on carcinogen metabolism.

Project Dates:
May 1984–May 1986.

Financial Support:
EPA (R-810451-01-0).

0782. HOWARD UNIVERSITY, Department of Zoology, 415 College Street, NW., Washington, D.C. 20059.

Project Title:
Hormonal Regulations of Environmental Carcinogenesis.

Principal Investigators:
Ampry, F.R.; Mohla, S.

Objective:
To (1) investigate effect of exogenous administration of estradiol on activating potential of certain tissues (kidney and liver) on model carcinogens; (2) investigate effect of administering diethyl stilbestrol and 1881 on activation potential of certain tissues on model carcinogens; (3) investigate role of steroid antagonists on ability of certain tissues to activate model carcinogens; and (4) investigate if steroid hormones will modulate metabolism of other nitrosamines (e.g., N-diethylnitrosamine, nitrososarcosine, N-nitrosomorpholine, N-nitrosopyrrolidine) of different chemical structures both enzymatically and mutagenetically.

Methods or Approach:
Animals were killed by cervical dislocation or by decapitation and tissues were prepared. In all studies, either *Salmonella* TA 98 or TA 100 was used to determine the mutagenic potential of the tissue. Data were expressed as the total number of revertants/plate. The test chemical in all instances was dimethylnitrosamine (DMN).

Results to Date:
Previous studies have indicated that liver S-9 fractions have the greatest potential to activate DMN. While the mutagenic potential of liver homogenates is neither age- nor sex-dependent; male S-9 fractions have a significantly greater potential to activate DMN than mature females, immature animals, and castrates. Testosterone treatment of mature females, immature animals, and castrates increases the potential of kidney S-9 fractions to biotransform DMN to levels seen in mature males. Experiments were performed to determine if estradiol will alter the mutagenic potential of mature male BALB/c mice kidney homogenates. Results of estradiol administration (0.1 μg/day for 10 days) indicated that (1) exogenous estradiol injections in female mice had no effect on mutagenic potential of any tissue homogenates, and (2) injecting males with estradiol had no effect on mutagenic potential of liver homogenates, but significantly lowered mutagenic potential of kidney homogenates. A threefold decrease in mutagenic potential of kidney S-9 fractions was observed.

Future Plans:
Future investigations will determine effects of administration of synthetic steroids on mutagenic potential of kidney and liver homogenates from various strains of mice and rats using model carcinogens and whether steroid hormones will modulate metabolism of other nitrosoamines of different chemical structures both enzymatically and mutagenically.

Financial Support:
NIH Minority Biomedical Research Support Program; NCI (2S0GRR08016).

0783. U.S. ENVIRONMENTAL PROTECTION AGENCY, 401 M Street, SW., Washington, D.C. 20460.

Project Title:
Risk Assessment of Passive Smoking.

Principal Investigators:
Repace, J.L.; Lowrey, A.H.

Objective:
To explore factors affecting the concentration of tobacco smoke in occupied spaces; and use information in risk assessment of passive smoking.

Methods or Approach:
An indoor air pollution model to predict concentrations of airborne tobacco tar and carbon monoxide has been developed and experimentally verified. The model was found to accurately predict experimental chamber measurements of Leaderer et al. for smoking rates ranging from 4 to 16 cigarettes/hour over effective ventilation rates ranging from 2.2 to 13.6 air changes/hour. It has also been found useful in understanding concentrations of respirable particles (RSP) observed in field surveys of smoking under natural conditions in homes and commercial buildings.

Results to Date:
Measurements of levels of RSP in public buildings where tobacco is smoked conclusively demonstrate that tobacco smoke inflicts substantial air pollution burdens on nonsmokers, far in excess of those encountered in smoke-free environments, outdoors, and in vehicles on busy commuter highways. RSP from tobacco smoke cannot be adequately controlled to within the levels of U.S. Air Quality Standards set for outdoor air under typical conditions of smoking occupancy and using standard ventilation rates set by the American Society of Heating, Refrigerating, and Air Conditioning Engineers (ASHRAE). Under typical conditions of ventilation, concentrations of ambient tobacco smoke encountered by nonsmokers can be approximated by an equilibrium model. The model, when combined with ASHRAE ventilation criteria, typical building occupancies, respiration rate tables, time budget studies, and surveys of the smoking policies of U.S. corporations and prevalence of smoking in the home, yields an exposure model that has been used to derive an estimated average exposure of the typical U.S. adult nonsmoker of 1.4 mg tar/day. When the exposure model is coupled with epidemiologic studies of passive smoking and lung cancer, a phenomenologic exposure-response relationship is derived. Using the exposure–response relationship, aggregate exposure to ambient tobacco smoke is estimated to produce about 5,000 lung cancer deaths/year in nonsmokers over 35 years of age. Mortality from passive smoking is estimated to be about two orders of magnitude higher than that estimated for carcinogens currently regulated as hazardous air pollutants under the Federal Clean Air Act. To achieve acceptable risk levels, the daily average concentration of tobacco tar for a typical office must not exceed 0.75 mg/m^3 air. At typical smoking occupancies for an office environment, achieving this standard would require impractical amounts of ventilation or prohibitive costs for air cleaning equipment. It appears that the only practical control measures are complete physical separation of smokers and nonsmokers on different ventilation systems or prohibition of workplace smoking.

Future Plans:
A comprehensive review of modeling and measurement of sidestreem smoke for epidemiologic purposes is planned.

Project Dates:
1976–continuing.

Financial Support:
EPA.

References:
(1) Repace, J.L.; Lowrey, A.H. *Modeling Exposure of Nonsmokers to Ambient Tobacco Smoke.* Prepared for presentation at the 76th Annual Meeting of the Air Pollution Control Association, Atlanta, Georgia, June 19-24, 1983, 22 pp. (2) Repace, J.L. "Effect of Ventilation on Passive Smoking Risk in a Model Workplace." In: Janssen, J.E. (Chairman). *Manage-*

ment of Atmospheres in Tightly Enclosed Spaces. Proceedings of an Engineering Foundation Conference, Santa Barbara, California, October 17-21, 1983. Atlanta, American Society of Heating, Refrigerating, and Air Conditioning Engineers, Inc., 1983, pp. 51-55. (3) Repace, J.L. "Consistency of Research Data on Passive Smoking and Lung Cancer." *Lancet* 2:506, 1984. (4) Repace, J.L.; Lowrey, A.H. "A Qualitative Estimate of Nonsmokers' Lung Cancer Risk From Passive Smoking." *Environment International* (In press). (5) Repace, J.L.; Lowrey, A.H. "An Indoor Air Quality Standard for Ambient Tobacco Smoke Based on Carcinogenic Risk." *New York State Journal of Medicine* (In press).

0784. USDA, ECONOMIC RESEARCH SERVICE, GHI Building, Washington, D.C. 20250.

Project Title:
Tobacco: Current Outlook and Situation, Supply, Demand, Use, and Price Analysis.

Principal Investigator:
Grise, V.N.
Objective:
To (1) appraise the current and prospective economic position of leaf tobacco and tobacco products; (2) identify and measure the influence of domestic and international economic factors on supply, demand, price, and use of tobacco and tobacco products; and (3) develop improved information and analyses for evaluating the effects of economic factors and assessing the economic position of tobacco and tobacco products.
Methods or Approach:
Statistical series are regularly assembled and compiled from many sources on production, stocks, total supplies, domestic utilization, foreign trade, and prices for individual types of tobacco; and on manufacture, consumption, foreign trade, and taxes of tobacco products. The effects of factors affecting supply, demand, utilization, and prices of tobacco and its products are described and quantitatively measured. The following aspects are analyzed: the growers' response to changing quantity and quality requirements; implications of supply responses for the support program and income to growers; trends in utilization of leaf tobacco and technological developments; and changes in consumers' and manufacturers' demand and the consequent effect on the market price structure of leaf, exports, overall crop prices, and income to growers.
Results to Date:
A projection of the domestic tobacco market through the 1980s emphasized a less favorable consumer attitude toward tobacco products; tobacco use in the United States is expected to continue to decline in per capita terms; with one-ninth more adult population, total tobacco use could rise slightly (4 percent) or decline slightly (8 percent) depending on the level of cigarette use.
Project Dates:
1930–continuing.
Financial Support:
ERS.

0785. VETERANS ADMINISTRATION MEDICAL CENTER, 941 North Capitol Street, NE., Washington, D.C. 20421.

Project Title:
Self-Actualization: Effect on Cancer Treatment Results.

Principal Investigators:
Martin, H.; Johnston-Earl, R.N.
Objective:
To (1) improve response to therapy and survival of inoperable cancer patients by making them active participants in treatment programs; (2) eliminate self-destructive habits including cigarette smoking and alcohol consumption; and (3) develop favorable psychological coping mechanisms (assertiveness training) to handle disease-related stress.
Methods or Approach:
Patients with squamous cell carcinoma of the head and neck or lung who have a confirmed histologic diagnosis, inoperable disease, no prior therapy, and ambulatory performance status will be given details of the program and will have the opportunity to decide whether or not to participate. Patients will be randomized to support or control groups. In the support group, close patient–staff interaction will be provided by the support team who will work with patients on a 1:1 or 1:2 basis, which is considered vital to success, since experience indicates that this particular patient population will not participate or derive benefit from group approaches. Members of the support team will aid the patient in understanding why self-abusive habits were initially begun, the effects on the body, and approaches to abstinence. Assertiveness training, relaxation therapy, imagery, therapeutic touch, video games, and recreational activities will be used to help patients end self-destructive habits and to gain positive attitudes and self-control. Both patient groups will receive identical antineoplastic chemotherapy. End points are response rates, especially complete response rate, and patient survival. Quality of life will be ascertained and physiological parameters of stress will be determined prior to, during, and at the end of the study period (8 to 12 weeks). Followup will continue indefinitely.
Results to Date:
Results are not yet available.
Financial Support:
VA.

Delaware

0786. E.I. DU PONT DE NEMOURS AND COMPANY, Employee Relations Department, Medical Division, N-11400, Wilmington, Delaware 19898.

Project Title:
The Effects of Carbon Monoxide Feedback on Smoking Cessation.

Principal Investigators:
Bertera, R.L.; Kiehne, E.C.; Telepchak, J.M.

Objective:
To determine whether carbon monoxide feedback can increase smoking cessation rates during clinics and reduce resumption of smoking at 6, 12, and 18 months postclinic.

Methods or Approach:
The project will be evaluated by a modified pretest–posttest control group design; groups will be assigned to either standard Freedom From Smoking clinics or the clinic plus carbon monoxide feedback by matching on the basis of age, sex ratio, and amount smoked at entry into the study. Smoking status will be determined by mailed survey 6, 12, and 18 months after end of the clinic (Lung Association Freedom From Smoking, seven sessions).

Results to Date:
Project is in a preliminary phase.

Project Dates:
August 1984–August 1987.

Financial Support:
E.I. du Pont de Nemours and Company.

Florida

0787. BIOFEEDBACK LABORATORY, 31 East Osceola Street, Stuart, Florida 33494.

Project Title:
Biofeedback: A Possible Substitute for Smoking. Experiments II and III.

Principal Investigator:
Griffith, E.E.

Objective:
To identify physiological variables that may contribute to maintenance of cigarette smoking; investigate the hypothesis that smoking frequency would decrease if individuals were trained via biofeedback procedures to increase 4-8 Hz occipital electroencephalograph activity as a substitute for the immediate physiological effects of smoking.

Methods or Approach:
A multiple baseline, across-subject design was used to identify variables in six smokers, during and immediately after smoking a cigarette.

Results to Date:
Results show that while actually smoking a cigarette, four subjects increased the percent of time they were producing 4-8 cycle/sec (Hz) brain waves, five increased heart rate, and all decreased 8-12 Hz activity. Immediately after smoking one cigarette, all demonstrated an increase in heart rate and four a decrease in skin temperature. There did not appear to be any specific consistent brain wave change across subjects. Two smokers, who were able to continue producing high levels of 8-12 Hz activity without use of biofeedback equipment, were able to quit completely at the end of an 8-month followup period.

Reference:
Griffith, E.E.; Crossman, E. "Biofeedback: A Possible Substitute for Smoking, Experiment I." *Addictive Behaviors* 8(3):277-285, 1983.

0788. CIGAREST QUIT-SMOKING CENTER, 2763 South Ridgewood Avenue, South Daytona, Florida 32019.

Project Title:
Multi-Modal Smoking Cessation Project.

Principal Investigators:
Brownfield, C.A.; Fanning, C.J.; Shaw, T.S.

Objective:
To (1) determine if the Sensation-Seeking Scale can be used as a predictor of outcome in smoking cessation treatment; (2) use multimethod approaches in combination with reduced environmental stimulation therapy (REST); and (3) test the efficacy of a self-help smoking cessation kit that utilizes REST as a catalyst.

Methods or Approach:
Smokers are given the Sensation-Seeking Scale prior to being treated for smoking addiction with five consecutive 1-hour daily sessions that include hypnosis, guided imagery, relaxation training, rapid smoking, suggestions for behavioral interventions, or aversive conditioning (low level electric shock); or in group and/or individual educational/informative sessions. Subjects also receive a kit with manual, reading materials, tape recordings, and other paraphernalia designed to augment the treatment or to serve as an independent self-help program. Followup sessions and booster programs are offered, with efficacy of maintenance planned via mail, postcard, and telephone inquiries.

Results to Date:
Although data are limited, sensation seekers seem to be more successful in enriched programs or combinations of treatment modalities, while sensation avoiders appear to require quicker withdrawal in a context of fewer instructions and less stimulation.

Future Plans:
The project plans to (1) enlarge the number to obtain respectable and quantifiable data; (2) refine materials; and (3) extend evaluation to include identifiable populations (males vs. females, sensation-seekers vs. sensation-avoiders, cardiovascular problems vs. pulmonary/respiratory illnesses).

Project Dates:
November 1984–continuing.

0789. FLORIDA INTERNATIONAL UNIVERSITY, Department of Marketing and Environment, Tamiami Trail, Miami, Florida 33199.

Project Title:
Public Policy and the Political Economy of the American Cigarette Industry: An Examination of Policy Alternatives in the Smoking–Health Controversy.

Principal Investigator:
Shepherd, P.L.

Objective:
To examine public health objectives in the area of smoking and health; examine policy options (governmental and nongovernmental) in relation to the political-economic structure of the American cigarette industry.

Methods or Approach:
The question for public health is no longer whether or not cigarette smoking in particular or tobacco use in general is harmful to health, nor even precisely how harmful, but rather what to do about the harm and how to prevent it in the future. Existing research and literature focuses overwhelmingly on servicing the problem through medical treatment or individual behavior modification/intervention and industry "nuts-and bolts" research (agricultural, manufacturing, tobacco chemistry). The political economy of the industry has largely been ignored and/or misunderstood. This study utilizes a political-economic approach to examine policy options and the structure, conduct, and performance of the industry.

Results to Date:
Examination of past and present policies suggest three major policy puzzles: (1) public health goals and objectives have shifted over time and have never been clear; (2) the link between policy and results is very tenuous; and (3) current initiatives seem unlikely to have intended effects. A more direct attack on the political-economic structure of the industry should be considered as well as regulatory and informational strategies at the margin of the industry. The industry is a paradigmatic case of oligopolistic transnational capitalism, and rapidly changing trends in the industry affect ability of outsiders to understand and intervene effectively. Smoking and health policy is a very difficult, complex issue for both governmental and nongovernmental actors interested in intervention. Either policy will have to be more creative and bold or expectations will have to be lowered.

Future Plans:
Recent trends in the industry (deregulation of agriculture, trade) will be examined to explore new alternative policies.

Project Dates:
January 1982–1986.

0790. FLORIDA INTERNATIONAL UNIVERSITY, Department of Marketing and Environment, Tamiami Trail, Miami, Florida 33199.

Project Title:
The Dynamics of the International Cigarette Oligopoly and the Denationalization of the Latin American Cigarette Industry.

Principal Investigator:
Shepherd, P.L.

Objective:
To (1) describe and explain development of the industrial organization of the transnational cigarette oligopoly; (2) explore how and why denationalization of Latin American cigarette industry occurred; and (3) examine some of the major effects of denationalization on industry structure, conduct, and performance.

Methods or Approach:
A political-economic approach is employed, utilizing a modified industrial organization framework to analyze structure, conduct, and performance. Focus is on (1) different levels and trends of concentration; (2) political, economic, and social significance of the industry; and (3) dynamics of cooperation and competition in the industry over time. It will also examine (1) international conduct and the process of denationalization; (2) evaluation of performance of the international oligopoly in Latin America; and (3) policy alternatives to improve performance in Latin America.

Results to Date:
The industry is highly concentrated and wields considerable political and economic power and influence in most markets. Highly diversified (transindustry) at home and highly international abroad (transnational), its structure illustrates the transition from single product, national oligopolies to multiproduct world oligopoly, perhaps a prototype of global corporate capitalism in the late 20th century. The history of cooperation and competition reveals a complex process of external threat and industry response. Competition is largely restricted to "marketing" (a misnomer) and product technology (both ultimately linked). Other areas of potential competition (labor costs, government policy prices, process technology, leaf tobacco) have been equalized, passing into the realm of cooperation, one of the more important sources of the industry's strength.

Future Plans:
Results will be analyzed in view of recent information (mid-1980s) to see if changes in structure, conduct, and performance have occurred since the late 1970s. Implications of the major conclusions need to be drawn for public policy toward the industry both in advanced capitalistic and less developed nations.

Project Dates:
January 1982–August 1986.

Financial Support:
Yale University, Center for Health Studies.

0791. MOUNT SINAI MEDICAL CENTER, Division of Pulmonary Disease, 4300 Alton Road, Miami Beach, Florida 33140.

Project Title:
Smoking and Breathing.

Principal Investigators:
Sackner, M.A.; Tobin, M.J.; Jenouri, G., et al.

Objective:
To (1) assess the pattern of inhalation in habitual smokers; (2) compare the assessment with the smokers' subjective estimation of inhalation, measured by a grading system and a visual analog scale, and (3) relate the depth of inhalation to current pulmonary function.

Methods or Approach:
The pattern of cigarette smoke inhalation was studied in 19 smokers with respiratory inductive plethysmography, a reliable unobtrusive ventilatory monitoring device.

Results to Date:
The mean volumes inhaled varied widely, from 0.27 to 1.97 L, with a group mean (±SD) of 0.79±0.45 L. Mean duration of smoke inhalation varied from 2.0 to 6.8 sec, with a group mean of 4.5±1.3 sec. An inhalation fraction was derived by dividing the inhaled volume by the vital capacity; this fraction varied from 0.09 to 0.47, with a group mean of 0.20±0.10. Subjects rated the depth that they inhaled smoke into their lungs on a visual analog scale and on a grading system. Correlation

between visual analog scale and inhalation fraction was poor (r = -0.15). Also, inhalation fraction bore no relationship to pack years of smoking or current pulmonary function. Such inaccurate assessment of inhalation pattern may help explain the poor correlation reported between cigarette smoke inhalation and severity of obstructive lung disease.

Project Dates:
July 1981–July 1982.

Financial Support:
NHLBI (HL10622).

References:
(1) Sackner, M.A.; Rao, A.S.V.; Birch, S., et al. "Assessment of Density Dependent Flow-Volume Parameters in Nonsmokers and Smokers." *Chest* 82(2):137-142, August 1982. (2) Sackner, M.A.; Rao, A.S.V.; Birch, S., et al. "Assessment of Time-Volume and Flow-Volume Components of Forced Vital Capacity." *Chest* 82(3):272-278, September 1982. (3) Tobin, M.J.; Jenouri, G.; Sackner, M.A. "Subjective and Objective Measurement of Cigarette Smoke Inhalation." *Chest* 82(6):696-700, December 1982.

0792. MOUNT SINAI MEDICAL CENTER, Division of Pulmonary Disease, 4300 Alton Road, Miami Beach, Florida 33140.

Project Title:
Breathing Pattern During and After Smoking Cigarettes.

Principal Investigators:
Tobin, M. J.; Schneider, A. W.; Sackner, M. A.

Objective:
To measure the effects of low- vs. high-tar cigarettes on inhalation patterns of smokers.

Methods or Approach:
The breathing patterns of 10 habitual smokers were monitored in the semirecumbent position with respiratory inductive plethysmography before and after smoking cigarettes. The subjects smoked a high tar content (HTC) and a low tar content (LTC) cigarette. The mean value and frequency histograms of minute ventilation, tidal volume (V_T), frequency, inspiratory time (T_I), fractional inspiratory time (T_I/T_{TOT}), and mean inspiratory flow (V_T/T_I) during baseline were compared with the values during and after smoking. Also, specific airway conductance (SG_{aw}) and multiple breath nitrogen washout were measured before and after smoking in six subjects.

Results to Date:
One group of smokers (n=4) had greatly increased mean baseline V_T/T_I (390±39 ml/s) compared with normal nonsmokers and another group (n=6) who had near normal V_T/T_I, 246±36 ml/sec. The first group (deep inhalers) had significantly higher mean inhalation fraction (volume of inhaled smoke and air/vital capacity: 0.25±.05). The second group had lower mean inhalation fraction of 0.14±0.03 (moderate inhalers). V_T/T_I decreased to 323±33 ml/s in the post-smoking period in deep inhalers, but increased to 345±65 ml/s in moderate inhalers during smoking. No systematic difference in V_T/T_I was noted between smoking high- and low-tar cigarettes, although the high-tar brand tended to have a greater effect on V_T/T_I. Deep inhalers showed a fall in V_T during and after smoking. Moderate inhalers showed a decrease in T_I/T_{TOT} during and after smoking. Measured in four moderate inhalers and two deep inhalers, SG_{aw} fell in all subjects after smoking HTC (19±8.7 percent) and LTC (13.9±10 percent) cigarettes. In moderate inhalers, increase in respiratory output (as reflected by increased V_T/T_I) combined with a reduction in T_I/T_{TOT} appears to reflect the respiratory center stimulant effect of nicotine directly or indirectly through bronchoconstriction. This contrasts with the reduced neural drive in deep inhalers that may relate to some overriding satiating effect of smoking.

Financial Support:
NHLBI (HL 10622).

Reference:
Tobin, M.J.; Schneider, A.W.; Sackner, M.A. "Breathing Pattern During and After Smoking Cigarettes." *Clinical Science* 63:473-483, 1982.

0793. UNIVERSITY OF FLORIDA, Department of Pediatrics, Box J-296, JHMHC, Gainesville, Florida 32610.

Project Title:
Effect of Exposure to Cigarette Smoke on Airway Reactivity and Frequency Dependent Compliance in Lambs.

Principal Investigator:
Hutchison, A.A.

Objective:
To assess the long-term effect of passive smoking on frequency dependent compliance (FDC) and airway responsiveness (AR) in 1-month-old lambs.

Methods or Approach:
Awake, 1-month-old lambs were intubated with a flexible bronchoscope and dynamic compliance (Cdyn) resistance of the lung (R_L) and functional residual capacity (FRC) were measured. Pleural pressure was measured with a Silastic ballon placed surgically in the right pleural space. Baseline airway reactivity to inhaled histamine, carbachol, and citric acid was measured in each of 11 lambs on 3 days by giving five breaths of increasing concentrations of the aerosol in a noncumulative fashion. The order of the three bronchoprovocation tests was randomized. The dose that would have caused a 35 percent reduction in Cdyn (ED_{35}Cdyn) or a doubling of R_L ($ED_{200}R_L$) was calculated. Six animals were exposed to cigarette smoke (CS) daily for 25 days using a ventilator to generate smoke and a 560 L exposure chamber. At each exposure, lambs breathed smoke from six cigarettes smoked at 15 minute intervals. Airway reactivity to each drug was remeasured on 3 separate days in the six CS lambs 1 to 7 days after CS and in the five nonsmoking lambs at an equivalent age. Frequency-dependent changes in dynamic compliance (FDC) were also measured in four of the CS lambs within 10 days and 4 to 6 weeks after CS. FDC was assessed by measuring Cdyn at increased respiratory rates of >100 that were achieved by warming the lamb with a heating blanket. FDC was considered present if Cdyn decreased to at least 65 percent of baseline with increased respiratory rate.

Results to Date:
Results showed that under baseline conditions, 6 of the 11 lambs did not respond to any of the three aerosols, 3 of 11 had a significant response to histamine, 2 of 11 responded to citric acid, and 3 to carbachol. One day after CS, four of the six lambs had increased reactivity to the aerosol tested, but by from 2 to 5 days after CS, the lambs were again nonreactive. Two of the six CS lambs remained nonresponders after exposure. FDC was present in all four CS lambs 10 days after exposure, but was not present at from 4 to 6 weeks after exposure. It is concluded that cigarette exposure in young lambs causes acute frequency-dependent decreases in dynamic compliance and, in some animals, increased airway reactivity.

Project Dates:
November 1983–June 1985.

Financial Support:
University of Florida; NHLBI (HL 30928-2); ALA of Florida.

0794. UNIVERSITY OF FLORIDA, Department of Clinical Psychology, Box J-165, Gainesville, Florida 32610.

Project Title:
Smoking Cessation and Relapse Prevention.

Principal Investigator:
Glaros, A.G.
Objective:
To examine efficacy of relapse prevention methods in smoking cessation programs, especially methods utilizing social skills training, cognitive-emotional skills training, and techniques derived from medical compliance literature.
Methods or Approach:
In study I, a relapse prevention module (social skills training) was added to a broad-spectrum smoking cessation program. A second group discussed coping strategies, but was not trained in coping with high-risk for smoking situations. A third group received standard treatment. Various smoking variables and social skills competence were utilized as dependent measures. In study II, cognitive-emotional training was contrasted with social skills training, and differing "time out from smoking" strategies were compared. In study III, short, intensive programs were contrasted with more traditional and lengthy smoking cessation approaches.
Results to Date:
In study I, social skills training lengthened the time to relapse but did not prevent relapse at followup. In study II, cognitive-emotional training was equally as effective as social skills training in preventing relapse. Also, time-out procedures in which the most difficult high-risk situations were eliminated first showed significantly greater cessation and relapse prevention than time-out procedures in which the most difficult high-risk for smoking situations were attempted late in the program. Study III results are not yet available.
Future Plans:
Investigation of the efficacy of in vivo procedures for smoking cessation and relapse prevention is currently underway.
Project Dates:
September 1982–July 1987.
Financial Support:
University of Florida; NIH.

0795. UNIVERSITY OF FLORIDA, Department of Clinical Psychology, Box J-165, Gainesville, Florida 32610.

Project Title:
Taste Preference and Discrimination.

Principal Investigator:
Glaros, A.G.
Objective:
To determine dimensions of taste and taste preference in smokers and nonsmokers under the effects of nicotine or tobacco.
Methods or Approach:
Smokers participated in a multidimensional scaling project utilizing popular, commercially available cigarettes. In a second study, preference for sweet and nonsweet substances is being examined in smokers, utilizing commercially available cigarettes.
Results to Date:
Smokers cannot reliably discriminate their regular cigarette from other cigarettes. Preference for cigarettes is strongly related to a sweet-bitter taste dimension, but not related to tar, nicotine, or carbon monoxide level. Results of the second study are not yet available.
Future Plans:
The effect of nicotine on taste preference among nonsmokers will be examined.
Project Dates:
July 1983–July 1987.
Financial Support:
University of Florida.

0796. UNIVERSITY OF FLORIDA, COLLEGE OF MEDICINE, Department of Psychiatry, Box J-256, JHMHC, Gainesville, Florida 32610.

Project Title:
An Epidemiologic Study of Alcohol Use, Problem Drinking and Alcohol Dependence Among an Aging Population.

Principal Investigators:
Warheit, G.J.; Adams, J.E.; Auth, J.B.
Objective:
To compare alcohol and tobacco consumption among the elderly, with particular attention to each respondent's history of smoking.
Methods or Approach:
A sample of 2,000 respondents (500 aged 18 to 59; 1,500 aged 60 or over) was drawn by random digit dialing in Alachua County, Florida. Interviews (at home), using a 280-item questionnaire, elicited information on sociodemographic background, social relationships, religion, physical health, diet, mental health, life events, alcohol use and history of use, other drug use, smoking and use of smokeless tobacco, current problems, and life satisfactions.
Results to Date:
As of February 1985, 1,300 respondents had been interviewed. Data for the first 650 subjects show that among the 79 males aged 18 to 29, 55.7 percent had never smoked, 22.8 percent are former smokers, and 21.5 percent are current smokers. Among the 126 aged 30 to 59, percentages were 35.7 percent, 31.0 percent, and 33.3 percent, respectively; for the 89 males 60 years of age or over, percentages were 23.6, 44.9, and 31.5, respectively. Percentages for the 88 females aged 18 to 29 were 62.5 percent never smokers, 15.9 percent ex-smokers, and 21.6 percent current smokers. In the group aged 30 to 59, percentages for the 139 females were 54.0, 20.1, and 25.9, respectively. For the those 60 years of age or over, 60.5 percent were never smokers, 25.8 percent were ex-smokers, and 13.7 percent were current smokers. Smokeless tobacco use by race and sex was as follows: 240 white males, 7.5 percent; 42 black males, 7.1 percent; 275 white females, 1.1 percent; 63 black females (all ≥ 60 years), 17.5 percent.
Future Plans:
Followup of 400 respondents selected from the original 2,000 will be conducted at yearly intervals for 4 years.
Project Dates:
July 1983–November 1990.
Financial Support:
NIAAA (P50AA05793).

0797. UNIVERSITY OF MIAMI, SPANISH FAMILY GUIDANCE CENTER, 747 Ponce De Leon Boulevard, Suite 303, Coral Gables, Florida 33134.

Project Title:
Family Effectiveness Training (FET).

Principal Investigator:
Szapocznik, J.
Objective:
To develop family effectiveness training (FET) that utilizes

both intervention and prevention strategies within the context of a psychoeducational modality that can be applied as part of prevention programs to reduce risk of drug abuse in adolescents.

Methods or Approach:
The basic test of the modality was accomplished by an experimental design of FET vs. a control condition (referred to as a minimum contact control (MCC) condition). Because of clinical and ethical considerations, it was necessary to add a clinical extension to the design that allowed for provision of the FET intervention to subjects who desired treatment, following assignment to the MCC condition. Having developed the clinical extension, a concern over repeated assessments was introduced and it became desirable to add further control conditions to test for the effect of repeated assessments. The final design became a Solomon Four Group design that experimentally tested for intervention and effects of assessment, and a clinical extension to the design was added for clinical and ethical considerations.

Results to Date:
In general, results suggest that the FET intervention/prevention modality was moderately effective in reducing the high risk syndrome in families with preadolescents. It is suggested that results would have been more definitive had the study used a simpler design with fewer cells and pretesting for all subjects. Areas of greatest effectiveness were in the ability of FET to bring about changes in parents' reports of behavior problems in the child. In addition, FET was effective in modifying resonance and structure in family interactions and reducing parents' reports of conflict in the family.

Project Dates:
May 1981–May 1983.

Financial Support:
NIDA (5R01DA2694).

0798. UNIVERSITY OF SOUTH FLORIDA, Department of Criminal Justice, Tampa, Florida 33620.

Project Title:
The Effect of Perceived Neighborhood Setting on Self-Reported Tobacco, Alcohol, and Marijuana Use Among Inner-City Minority Junior High School Youth.

Principal Investigators:
Blount, W.R.; Dembo, R.

Objective:
To study the relationship between an inner-city youth's perception of the neighborhood in which he lives and the correlates of his own drug-taking behavior.

Methods or Approach:
Data were gathered in the second wave of a two-part survey of youths attending a South Bronx, New York City, junior high school. More girls than boys were represented and most of the youths (average age, 13 years) were Puerto Rican or black. The majority lived with both parents; 38 percent claimed to reside with their mother. Questions were included on parents' educational and occupational level. Over 97 percent of students in class at the time of the survey participated, representing 78 percent of the 1,344 students enrolled in the school. Factor scores were developed and were derived in such a manner that the higher the score, the greater the adherence to the attitude, perception, or behavior named by the cluster. An extensive range of questions were used to probe the youths' orientations to, and involvement in, various aspects of their neighborhood. A variety of measures were also used to probe the degree to which drug use was a part of the social networks in which the youths operated, and 13 items tapped views of the degree of "toughness" and drug use existing in the neighborhood. Subjects were asked to respond concerning use of alcohol, marijuana, LSD or similar substances, depressants, narcotics, solvents, stimulants, and tobacco.

Results to Date:
The relationship between neighborhood setting and drug use appears to be drug specific. For alcohol and tobacco, a knowledge of peer use was highly predictive of personal use, independent of how tough or drug-involved the neighborhood was thought to be. Personal marijuana use was quite dependent on neighborhood perceptions, becoming more predictive as the neighborhood was perceived as tougher and more drug involved. Knowledge of spare-time activities was predictive of tobacco and marijuana use (independent of neighborhood) but not predictive for alcohol use. Data suggest that because the relationships are complex, intervention/prevention strategies must not only be drug specific, but also must proceed on many fronts simultaneously. In a published report, suggestions are offered (along with a discussion of findings) that may help identify nonusers and users in the same population.

References:
(1) Blount, W.R.; Dembo, R. "The Effect of Perceived Neighborhood Setting on Self-Reported Tobacco, Alcohol, and Marijuana Use Among Inner-City Minority Junior High School Youth." *International Journal of the Addictions* 19(2):175-198, 1984. (2) Dembo, R.; Schmeidler, J.; Burgos, W., et al. "Environmental Setting and Early Drug Involvement Among Inner City Junior High School Youths." *International Journal of the Addictions* (In press).

0799. UNIVERSITY OF SOUTH FLORIDA, 4202 East Fowler Avenue, Tampa, Florida 33620.

Project Title:
Everyday Stressors and Relapse in Ex-smokers.

Principal Investigator:
Shiffman, S.

Objective:
To investigate the relationship between relapse in ex-smokers and small scale everyday stressors and positive experiences; examine effects of various strategies for coping with stress and for coping with temptations to smoke.

Methods or Approach:
Recidivists often identify stress as the precipitant of relapse; other studies have suggested that major life events may play some role in promoting relapse. Study focus is on an intermediate level or definition of stress. The importance of performing a coping response when faced with temptation has been shown. This perspective is broadened to examine what ex-smokers do to prevent or recover from lapses and how they generally cope with stress. The prospective longitudinal study of 150 to 200 smokers who are planning to quit smoking will assess smoking history and stress, withdrawal symptoms, and coping patterns at baseline. All subjects will be interviewed repeatedly over periods ranging from 3 weeks to 3 months, depending on course of smoking cessation. Measures will include "hassles" and "uplifts" scales, withdrawal symptoms scales, and measures of coping style.

Results to Date:
Preliminary results suggest that everyday stress is involved both in precipitating relapse crises in which abstinence is threatened and in promoting actual relapse. One of the most striking aspects of preliminary data is the frequency of at least temporary lapses in abstinence even among those who are ultimately successful in quitting smoking.

Project Dates:
September 1984–August 1985.
Financial Support:
NIDA (1R03DA03491-01A1).

0800. VETERANS ADMINISTRATION MEDICAL CENTER, 1000 Bay Pines Boulevard, North, Bay Pines, Florida 33504.

Project Title:
Smoking and Lung Cancer: Feasibility Study of a Diagnostic Test to Identify Persons at High Risk.

Principal Investigators:
Samis, H.V., Jr.; Frankel, J.W.
Objective:
To determine in vitro susceptibility to viral transformation of human cultured fibroblasts with Kirsten Murine Sarcoma virus (KiMSV) for people with diagnosed cancers and those without diagnosed cancers.
Methods or Approach:
It is anticipated that a procedure may be developed by means of virus titration, that may eventually make it possible to predict the probability that an individual will develop cancer. Fibroblasts obtained from human skin biopsies from individuals with and without clinically demonstrable cancer are treated with Kirsten Murine Sarcoma virus (KiMSV) and transformation scored as to the virus titer that elicits transformation of the fibroblasts.
Results to Date:
Differences in susceptibility to KiMSV-induced transformation of human skin biopsy for individuals with lung cancer and those without was found to be significant at $p=0.001$. Studies using blind coded cultures have to date shown 95 percent correspondence with original findings. Transformation studies are continuing with cells from individuals with different types of cancer. It is anticipated that the code for these cultures will be broken during January 1985. Subcultures have been stored in anticipation of the development of future projects dealing with the mechanism of KiMSV-induced transformation of cultured human fibroblasts.
Financial Support:
VA.

0801. VETERANS ADMINISTRATION MEDICAL CENTER, Archer Road, Gainesville, Florida 32608.

Project Title:
Effects of Chronic Tobacco Smoke Exposure on Functions of Rat Lung.

Principal Investigator:
Harris, J.O.
Objective:
To gain insight into the pathogenesis of lung diseases associated with cigarette smoking by investigating effects of chronic smoke exposure on important functions of the pulmonary alveolar macrophage (PAM) in an animal model.
Methods or Approach:
Protein biosynthesis, secretory function, phagocytic functions, and plasma membrane characteristics of PAMs will be evaluated in smoke-exposed and control rats. Two-dimensional gel electrophoresis (isoelectrofocusing followed by SDS-polyacrylamide gel electrophoresis) will be utilized to qualitate and quantitate radiolabeled PAM proteins. In vitro cell cytotoxic assays have been employed to quantitate radiolabeled PAM proteins and to quantitate cytotoxic factors secreted by PAMs. The acridine orange assay is used to quantitate phagosome-lysosome fusion in PAMs challenged with viable yeast organisms. Fluorescence spectroscopy, using diphenyl hexatriene as a membrane probe, has been used to estimate membrane fluidity of PAM plasma membranes. Scanning electron microscopy is used to evaluate PAM surface morphology.
Results to Date:
Exposure to cigarette smoke produces a number of changes in PAM; cells have altered surface morphology, and PAM exposed to the gaseous phase of cigarette smoke have decreased membrane fluidity. The ability of smoke-exposed PAM to endocytose yeast organisms is not decreased, but transfer of lysosome contents to the yeast-containing phagosome is significantly decreased. Smoke-exposed PAM incorporate more radiolabeled amino acid into protein, but are deficient in secretion of cytotoxic factors. Findings could explain increased incidence of respiratory infection and decreased cancer surveillance in cigarette smokers.
Financial Support:
VA.

0802. VETERANS ADMINISTRATION MEDICAL CENTER, Archer Road, Gainesville, Florida 32608.

Project Title:
The Effects of Cigarette Smoking on the Structure and Function of Pulmonary Alveolar Macrophages.

Principal Investigators:
Gonzalez-Rothi, R.J.; Harris, J.D.
Objective:
To identify and compare alveolar macrophage subpopulations from smoking and nonsmoking human subjects with respect to morphologic and functional characteristics.
Methods or Approach:
Ten healthy, young smokers and 10 healthy, young nonsmokers will undergo bronchoalveolar lavage by fiberoptic bronchoscopy. Alveolar macrophages thus retrieved will be studied and compared with respect to in vitro morphologic and functional characteristics. Human alveolar macrophages obtained by lung lavage will be fractioned into different subgroups by Percoll density gradient centrifugation. Each subgroup will be examined morphologically by lytochemical staining and by scanning electron microscopy. Also, cells from respective subgroups will be examined with functional studies that include phagocytosis, phagolysosome fusion using vital staining fluorescent microscopy, and chemotaxis using the agarose well technique. Morphologic and functional subpopulation profiles of smokers will be compared with those of nonsmokers.
Results to Date:
Project is in a preliminary phase.
Financial Support:
VA.

0803. VETERANS ADMINISTRATION MEDICAL CENTER, Archer Road, Gainesville, Florida 32608.

Project Title:
Effect of Cigarette Smoking on the Tumoricidal Potential of Human Lung Macrophages.

Principal Investigators:
Gonzalez-Rothi, R.J.; Harris, J.O.; Flick, D.
Objective:
To determine whether smoke component(s) suppress pulmonary alveolar macrophages (PAM) tumor cytotoxic functions in human smokers leading to defective control of oncogenesis

in lung tissues chronically in contact with inhaled tobacco carcinogens.

Methods or Approach:

Cigarette smoking is the strongest etiological risk factor for development of lung cancer in humans. Despite the obvious presence of known carcinogens in inhaled tobacco smoke, little is known of the mechanisms(s) by which smoking might induce lung neoplasms. Smoking is known to produce significant structural and functional alterations in PAMs of humans and animals, and recent evidence suggests that these immunologically crucial resident lung cells may participate in tumor surveillance mechanisms in the lung. Based on preliminary studies using an accepted animal model of chronic in vivo cigarette smoke inhalation, in vitro production of a soluble tumor cytotoxin by PAM of smoke-exposed rats is significantly depressed compared with cells from nonsmoking controls. Research will consist of obtaining PAM by bronchoalveolar lavage from smoking and nonsmoking human volunteers and from smokers with primary lung cancer. PAM will be used as effector cells, cultured in vitro, and culture supernatants will be examined for ability to lyse adherent target cell monolayers from a transformed cell line and from various human tumor cell lines. Cytotoxicity will be quantitated using a sensitive photometric technique, and in vitro cytotoxin production by PAM of human smokers, nonsmokers, and smokers with lung cancer will be compared.

Results to Date:

Results are not yet available.

Financial Support:

VA.

Georgia

0804. USDA, AGRICULTURAL RESEARCH SERVICE, R.B. RUSSELL AGRICULTURAL RESEARCH CENTER, Athens, Georgia 30601.

Project Title:

Reduction of Lipid Components in Tobacco.

Principal Investigator:

Schepartz, A.L.

Objective:

To (1) study biochemical mechanisms involved in lipid synthesis in the leaf; (2) determine means of inhibition; and (3) develop methods to degrade lipids during leaf processing, thus reducing contribution of lipids as precursors of smoke tumorigens.

Methods or Approach:

Biochemical systems that synthesize lipids in leaf will be investigated, and enzyme inhibition will be studied. Methods will be developed for lipid degradation during curing or aging and both techniques will be applied to reduce lipid content. Smoke and leaf analyses, pyrolysis, and bioassay will be correlated to determine effect of lipid reduction on the safety of the smoke. Tobaccos produced by new methods of genetics, culture, curing and aging designed to yield low-lipid tobaccos with lower tumorigenicity of the smoke will be evaluated.

Results to Date:

Research on the biochemistry of green tobacco has resulted in the finding of an enzyme system that is capable of synthesizing solanesol. Solanesol was synthesized from mevalonic acid through a strongly bound enzyme–substrate complex (Km = 0.0019 M) during a 24-hour incubation. Experiments were conducted to determine optimum reaction conditions, and previous methods for the analytical determination of solanesol were modified. Research on the ozonization of tobacco to effect decomposition of leaf lipids was continued on a pilot-plant scale. Experiments were conducted on aqueous slurries of tobacco in large PVC reaction columns, with ozone introduction at the bottom. To evaluate column agitation and ozone contact, samples were removed at intervals from each third of the columns. After two hours of treatment, solanesol was reduced 38 percent in the lower third, 32 percent in the middle third, and 17 percent in the upper third of the reaction columns, indicating a height effect. At the same time, unsaturated fatty acids were reduced by 28 percent, 37 percent, and 14 percent, and total sterol reductions were 37 percent, 49 percent, and 63 percent, respectively, from bottom to top. In a study of the curing process, variations in free lipids were compared with total lipids in a flue-cured tobacco.

Project Dates:

November 1979–May 1984.

Financial Support:

USDA (6612-20881-004D).

Reference:

Schepartz, A.I.; Ellington, J.J.; Wilson, R.L., et al. "An Analysis of the Variation in Leaf Lipids During the Curing of Flue-Cured Tobaccos." *Tobacco Science* 26:47-50, 1982.

0805. USDA, AGRICULTURAL RESEARCH SERVICE, Tifton, Georgia 31794.

Project Title:

Evaluation of Growth Regulators for Reducing Chemical Residues in Tobacco Leaf and Smoke.

Principal Investigator:

Hammons, R.O.

Objective:

To evaluate new growth regulators and other means to reduce exogenous chemical residues in tobacco leaf and smoke.

Methods or Approach:

Sucker control by growth regulators will be investigated to reduce pesticide residues and to find new compounds that are not hazardous to health. Nonchemical pest control methods via genetic means will be evaluated in field trials to find genotypes in which the finished product is less hazardous to health. New genotypes that offer natural resistance to insects, allowing reduced insecticide use, and thereby reduce hazardous effects on health and environment will be tested.

Results to Date:

Five compounds at this location in the preliminary and advanced regional sucker control test have shown good sucker control, yield, and quality results as compared with the fatty alcohol KMH control. These compounds are CMH by Mitsubishi, DS 40825 by Diamond Shamrock, PH 3019 as a dual application, and PH 3020 by Duphar and PPG 575 as a dual application by PPG Industries. Over 400 breeding lines, roses and cultivars of tobacco were screened under field conditions to identify insect-resistant germplasm. Two multiple disease-resistant varieties, NC 50USDA and NC 7567, were declared eligible for variety release by the Regional Variety Evaluation Committee. The application of leaf wash materials containing alpha and beta duvatreine-ols and alpha and beta duvatreinediols from NC 2326 to Ti 1112, a budworm resistant variety, induced oviposition.

Project Dates:
January 1975–March 1986.

Financial Support:
USDA (6602-20880-001D).

References:
(1) Seltmann, H.; Priest, J.S.; Whitty, E.B., et al. *Regional Tobacco Growth Regulator Test Flue-Cured, 1982.* USDA ARS Southern Region, Mid-Atlantic Report (In press). (2) Herzog, G.A.; Stephenson, M.G. "Official Variety Test–Insect Screen."*1982 Georgia Tobacco Research and Extension Report.* University of Georgia, Pub. 106, pp. 60-61, 1983. (3) Csinos, A.S.; Stephenson, M.G. "Effect of Crop Residue on *Sclerotinum rolfsii* Seedling Disease of Tobacco." *1982 Georgia Tobacco Research and Extension Report.* University of Georgia, Pub. 106, pp. 88-80, 1983. (5) Stephenson, M.G. *Flue-Cured Variety Test. 1982 Field Crops Performance Tests.* University of Georgia, College of Agriculture Research Report, 1983.

0806. USDA, AGRICULTURAL RESEARCH SERVICE, R.B. RUSSELL AGRICULTURAL RESEARCH CENTER, Athens, Georgia 30601.

Project Title:
Pyrolytic Studies on Compounds Related to Flavor, Aroma and Biological Properties of Tobacco Smoke.

Principal Investigators:
Schlotzhauer, W.S.; Chortyk, O.T.

Objective:
To determine the leaf precursor and modes of formation of both the hazardous and the aroma-related compounds of tobacco smoke; evaluate new tobacco germplasm and tobaccos produced by new agronomic/curing methods in order to guide development of a safer tobacco.

Methods or Approach:
Tobacco isolates, leaf extracts, or leaf constituents (lipids, carbohydrate, pectins, lignins, phenolic constituents, acids, alkaloids, proteins, or other components) were pyrolyzed to determine the leaf precursors of hazardous compounds that occur in the condensate (PAH, quinones, phenols, nitrosamines, and aza-arenes) and vapor phase (carbon monoxide, hydrogen cyanide, ammonia, nitrogen oxides, aldehydes, and nitrosamines) of tobacco smoke. Similarly, potential leaf precursors of the flavor/aroma constituents of smoke (carbonyls, esters, terpenes, and furans) will be examined and flavor/aroma profiles (by glass capillary GC) will be developed. Methods of trapping volatiles will be examined. Pyrolytic product–precursor results will be used to guide genetic and agronomic developments of a safer tobacco. Analytical methods will be used to evaluate new germplasms.

Results to Date:
Pyrolytic studies have been conducted to determine the effects of the homogenized leaf curing (HLC) process on tobacco smoke composition. Pyrolyzate nicotine, volatile phenols, and neophytadiene increased with time in the field, while catechol and fatty acids declined. Incubation of the final HLC product resulted in little change in smoke products. The amount of air available during the slurring process had significant effects on all pyrolyzate compounds. Increased pH resulted in higher alkaloid levels and lower catechol and fatty acid yields. PAH analyses from flue-cured, HLC, and deproteinated HLC tobaccos pyrolyzates showed higher levels of PAH components from HLC vs. flue-cured tobaccos. Nitrosonornicotine levels were significantly lower in HLC, while volatile nitrosamines were generally lower in HLC vs. flue-cured pryolyzates. Studies were completed on determination of the effects of varied human smoking behavior, using alterations in machine smoking conditions, on yield of total particulate matter (TPM), nicotine, and selected major smoke constituents. The data demonstrated that increases in intensity, duration, and frequency of puffing over standard (FTC) smoking conditions were accompanied by significant increases in TPM and smoke compounds. Similar effects were observed when filter tipping paper perforations were artificially obstructed.

Project Dates:
November 1979–November 1982.

Financial Support:
USDA (6612-20881-002D).

References:
(1) Schlotzhauer, W.S.; Martin, R.M.; Snook, M.E., et al. "Pyrolytic Studies on the Contributions of Tobacco Leaf Constituents to the Formation of Smoke Catechols." *Journal of Agricultural Food Chemistry* 30:373-374, March-April 1982. (2) Schlotzhauer, W.S.; Chortyk, O.T. "Effects of Varied Smoking Machine Parameters on Deliveries of Total Particulate Matter and Selected Smoke Constitutents from an Ultra Low-Tar Cigarette." *Journal of Analytical Toxicology* 7(2):92-95, March-April 1983.

0807. AUGUSTA VETERANS ADMINISTRATION MEDICAL CENTER, Psychology Service (116BU), Augusta, Georgia 30910.

Project Title:
Stressful Life Events and Smoking Cessation: A Retrospective Study of Successful Quitters.

Principal Investigators:
Nolan, W.P.; Arena, J.G.; Bennett, G.

Objective:
To determine the impact of stressful life events on decision to quit smoking; determine impact of smoking cessation on other changes in lifestyle and/or life structure.

Methods or Approach:
A survey will be conducted of a diverse sample of approximately 1,000 ex-smokers who have remained abstinent from cigarettes and other tobacco products for at least 1 year. A questionnaire has been designed to solicit detailed information about (1) smoking history; (2) events precipitating the decision to quit; (3) methods used to quit; (4) concurrent life changes; and (5) relative role of social, medical, and economic reinforcers. It is hypothesized that individuals may be more likely to quit during periods of relative turmoil rather than during periods of relative stability in their lives.

Results to Date:
Project is in a preliminary phase.

Project Dates:
January 1985–December 1985.

Financial Support:
VA.

0808. CENTERS FOR DISEASE CONTROL, PREGNANCY EPIDEMIOLOGY BRANCH, Building 1, Room 4423, Atlanta, Georgia 30333.

Project Title:
Smoking and Your Pregnancy.

Principal Investigators:
Berman, S.M.; Hogue, C.J.R.

Objective:
To increase awareness among women of the smoking-related risks during pregnancy.
Methods or Approach:
Too few women are aware of the risks that smoking poses for themselves and for their fetuses. If more pregnant women were aware of smoking-related risks, more of them might quit during pregnancy. A review of the relevant literature has been conducted and a publication is being prepared that will deal with why more women are not aware of the smoking-related risks. The material will be accessible to the general public.
Project Dates:
June 1984–March 1985.
Financial Support:
CDC.

0809. CENTERS FOR DISEASE CONTROL, CENTER FOR HEALTH PROMOTION AND EDUCATION, Division of Reproductive Health, Pregnancy Epidemiology Branch, 1600 Clifton Road, Building 1, Room 4419, Atlanta, Georgia 30333.

Project Title:
Premature Rupture of Membranes and Smoking During Pregnancy.

Principal Investigators:
Sappenfield, W.M.; Hogue, C.J.R.; Buehler, J.W., et al.
Objective:
To study the association of smoking with premature rupture of membranes in preterm delivery.
Methods or Approach:
A case–control study will be conducted, using data from the 1980 National Natality Survey, to compare infants that weighed <2,500 g and were preterm with premature rupture of membranes with infants that weighed >2,500 g and were term deliveries without premature rupture of membranes.
Results to Date:
Results are not yet released, but smoking appears to double the risk of preterm delivery with premature rupture of membranes.
Project Dates:
September 1984–March 1985.
Financial Support:
CDC.

0810. CENTERS FOR DISEASE CONTROL, Building 1, Room 3071, Atlanta, Georgia 30333.

Project Title:
Carter Center Health Policy Project.

Principal Investigators:
Amler, R.; White, C.C.
Objective:
To assess overall burden of morbidity and mortality for the United States for a 1980 base year; determine proportion of preventable morbidity and mortality attributable to major health risks, including smoking, alcohol, and injury.
Methods or Approach:
Using data from the Carter Center Health Policy Project compiled by consultants for 14 health problem areas, the portion of morbidity and mortality attributable to known, preventable health risks was determined. Compiled data were edited for internal consistency, insuring use of the same measures of morbidity and mortality, and preventing multiple counting of deaths.
Results to Date:
Tobacco is responsible for more deaths in the United States than any other single factor. It is the leading cause of preventable mortality both in total deaths and in years of life lost before age 65. Alcohol is the second leading cause of unnecessary mortality in potential years of life lost before age 65. Other important causes of preventable, premature mortality include injury, unintended pregnancy, improper nutrition, lack of screening and appropriate preventive services, and uncontrolled hypertension.
Project Dates:
January 1984–June 1985.
Financial Support:
Emory University, Carter Center.

0811. CENTERS FOR DISEASE CONTROL, COSTA RICAN DEMOGRAPHIC ASSOCIATION, Atlanta, Georgia 30333.

Project Title:
Costa Rica Evaluation of DMPA.

Principal Investigators:
Oberle, M.W.; Rosero, L.
Objective:
To compare use of Depo-Provera (DMPA) between women with breast cancer or cervical cancer and controls.
Methods or Approach:
A case–control study was conducted in Costa Rica to compare use of DMPA among women with breast cancer or cervical cancer and population-based controls. Smoking will be evaluated as an independent risk factor. The women surveyed were between the ages of 25 and 59.
Results to Date:
Data has been collected on 189 breast cancer cases, 731 cervical cancer cases, and 872 controls. Results are not yet available.
Project Dates:
June 1984–July 1986.
Financial Support:
CDC; USAID; Family Health International.

0812. CENTERS FOR DISEASE CONTROL, EPIDEMIOLOGIC STUDIES BRANCH, Division of Reproductive Health, Building 1, Atlanta, Georgia 30333.

Project Title:
Smoking and Endometrial, Ovarian, and Breast Cancer.

Principal Investigators:
Rubin, G.; Tyler, C.W.; Franks, A.L.; Stroup, N.
Objective:
To determine whether smoking is associated with endometrial, ovarian, or breast cancer.
Methods or Approach:
A multicenter, population-based, case–control study will be conducted.
Results to Date:
Overall, smoking was not found to be associated with any of the cancers studied.
Future Plans:
Data on subgroups will be analyzed.
Financial Support:
NICHD.

0813. CENTERS FOR DISEASE CONTROL, Building 3, Room 121, Atlanta, Georgia 30333.

Project Title:
The Behavioral Epidemiology of Smoking and Exercise.

Principal Investigators:
Powell, K.E.; Casperson, C.; White, C., et al.

Objective:
To explore the relationship between participation in vigorous physical activity and smoking behavior.

Methods or Approach:
Data from the Institute of Aerobics Research, behavioral risk factor surveys, and other community or national data sets are used to compare physical activity level with smoking behavior. Physical activity is measured in various ways, including kilocalories expended, hours spent, and frequency of participation. Activities included vigorous and nonvigorous leisure time activities, occupational physical activity, and household activity.

Results to Date:
Preliminary results suggest a modest but significant relationship between the energy expended in vigorous exercise activity and smoking/nonsmoking behavior. Smoking prevalence among nonexercisers is about 35 percent; among active exercisers, prevalence is about 28 percent.

Future Plans:
Further analysis using different measures and definitions will be used to explore relationships between exercise and physical activity and smoking behavior.

Project Dates:
July 1984–June 1986.

Financial Support:
CDC.

0814. CENTERS FOR DISEASE CONTROL, Building 3, Room 121, Atlanta, Georgia 30333.

Project Title:
Carter Center Health Policy Project: Cardiovascular Disease.

Principal Investigators:
Tolsma, D.; White, C.C.; Haynes, S.

Objective:
To (1) determine overall burden of cardiovascular disease (CVD) morbidity and mortality; (2) assess preventable or unnecessary portion of CVD based on existing knowledge and technology; and (3) determine portion of preventable CVD morbidity and mortality attributable to known risk factors (smoking, high blood pressure, elevated serum cholesterol, glucose intolerance, and lack of exercise).

Methods or Approach:
National data for 1980 were used to quantitate burden of morbidity and mortality from CVD. Multiple regression analysis, using equations from the UCLA Risk Factor Update Project and the Framingham study, was used to determine attributable risk for factors studied.

Results to Date:
Data indicate that of total CVD mortality, 16 percent is attributable to smoking, 30 percent to systolic blood pressure ≥ 140 mm Hg, 10 percent to serum cholesterol ≥ 220 mg/dL, and 14 percent to glucose intolerance. In terms of potential years of life lost before age 65, 31 percent can be attributed to smoking, 18 percent to high blood pressure, 9 percent to elevated serum cholesterol, and 4 percent to glucose intolerance.

Project Dates:
March 1984–June 1985.

Financial Support:
Emory University, Carter Center.

0815. CENTERS FOR DISEASE CONTROL, DIVISION OF NUTRITION, Building 3, SB 59, 1600 Clifton Road, NE., Atlanta, Georgia 30333.

Project Title:
Pregnancy Nutrition Surveillance System.

Principal Investigator:
Wong, F.

Objective:
To monitor nutritional status of pregnant women; investigate association of nutrition and other risk factors (i.e., smoking) with birth weight.

Methods or Approach:
Data is collected on low income pregnant women who attend publicly supported clinics. Data, including information on height, weight, hematocrit, hemoglobin, vitamin/mineral consumption, blood pressure, smoking, prepregnancy weight, date of birth, and racial/ethnic group. Information is included with birth outcome and sent by States for analysis via the Pregnancy Nutrition Surveillance System.

Results to Date:
In 1984-1985, 18 States and territories are participating in the system. Annual reports are published.

Future Plans:
There are tentative plans to expand the system to include additional behavioral risk factor data such as smoking and alcohol consumption prior to, during, and after pregnancy. This will allow for additional investigations of risk factors associated with low birth weight infants and evaluation of behavioral changes associated with pregnancy. The feasibility of linkage to birth and death certificates may also be explored.

Project Dates:
1979–continuing.

Financial Support:
CDC.

0816. CENTERS FOR DISEASE CONTROL, CENTER FOR HEALTH PROMOTION AND EDUCATION, Building 3 SB12, Atlanta, Georgia 30333.

Project Title:
Behavioral Risk Factor Surveillance System.

Principal Investigators:
Hogelin, G.; Gentry, E.

Objective:
To determine prevalence of major behavioral risk factors in selected States.

Methods or Approach:
Behavioral risk factors investigated include cigarette smoking, alcohol misuse, seatbelt usage, hypertension treatment compliance, overweight, and physical activity. Cigarette smoking data are collected on present use, number of cigarettes consumed/day, attempts to quit, and a number of demographic items. At present, 23 States and the District of Columbia participate in the system. Data are collected by telephone surveys. One adult per household is interviewed by a standard questionnaire (for analytic comparability). The 10-minute interviews are typically conducted during evenings and weekends, 1 week each month. Data are aggregated across 12 months of collection for annual estimates.

Results to Date:
The most recent data (1982) showed prevalence of cigarette smoking in U.S. adults to be 31.5 percent (34.0 percent in males, 29.1 percent in females). State prevalence ranged from a low of 22.1 percent in Kansas to a high of 37.7 percent in North Carolina.

Future Plans:
Data collection will continue and additional States will probably be added to the system.
Project Dates:
January 1983–continuing.
Financial Support:
CDC; OSH; NIAAA.

0817. EMORY UNIVERSITY, YERKES REGIONAL PRIMATE RESEARCH CENTER, Division of Behavioral Biology, Atlanta, Georgia 30322.

Project Title:
Behavioral and Physiological Concomitants of Drug Abuse.

Principal Investigator:
Byrd, L.D.
Objective:
To (1) determine the effects selected drugs can have on the central nervous system of conscious nonhuman primates by studying the effects of the drugs on conditioned behavior in squirrel monkeys and chimpanzees; (2) assess the effects these drugs can have on heart rate, blood pressure, and temperature at doses that have effects on behavior mediated via the central nervous system; and (3) study whether the behavioral, cardiovascular, or thermoregulatory effects can be enhanced, diminished, or blocked by other drugs and chemical substances or by behavioral procedures.
Methods or Approach:
Experiments will be conducted in squirrel monkeys surgically prepared under sterile conditions with chronically indwelling arterial and venous catheters and in chimpanzees trained to accept intramuscular injections. Protocols will utilize the direct measurement of systemic arterial blood pressure and heart rate as indices of cardiovascular activity, the direct measurement of colonic temperature as an index of thermoregulatory activity, and operantly conditioned psychomotor behavior as a measure of central nervous system activity. The administration of drugs, including nicotine, prior to or during the daily behavioral session permits evaluation of the drug effects on the central nervous system and selected physiological systems.
Results to Date:
Results are not yet available.
Project Dates:
September 1981–1984.
Financial Support:
NIDA (DA-01161); NIH (RR-00165).

0818. EMORY UNIVERSITY, SCHOOL OF MEDICINE, Department of Anatomy, Atlanta, Georgia 30322.

Project Title:
Influence of Steroid Hormones on Spontaneous Motor Activity in Mice.

Principal Investigator:
Hatchell, P.C.
Objective:
To (1) clarify the steroid hormonal influence on nicotine's motor effects in mice by modifying the hormonal content of tested mice; (2) establish the baseline motor activity after saline treatment and motor activity after nicotine administration in intact animals; (3) determine activity levels after nicotine and saline treatment in gonadectomized animals; and (4) assess the effect of exogenously administered male and female steroid hormones on nicotine's motor effects in gonadectomized animals.
Methods or Approach:
The influence of endogenous steroid hormones on nicotine motor effects will initially be assessed by comparing the motor activity in a Y-maze after nicotine administration in intact male and female inbred mice with the motor activity after nicotine treatment in gonadectomized animals (castration in males and ovariectomy in females). Additional control groups of intact and gonadectomized males and females will be used to assess baseline motor activity levels after saline injection. Subsequently, gonadectomized animals will be treated exogenously with either estradiol (in females) or testosterone (in males), followed by nicotine or saline administration and motor activity assessment.
Results to Date:
Results are not yet available.
Project Dates:
January 1983–1984.
References:
(1) Hatchell, P.C.; Collins, A.C. "Influences of Genotype and Sex on Behavioral Tolerance to Nicotine in Mice." *Pharmacology, Biochemistry and Behavior* 6(1):25-30, January 1977. (2) Hatchell, P.C.; Collins, A.C. "The Influence of Genotype and Sex on Behavioral Sensitivity to Nicotine in Mice." *Psychopharmacology* 71(1):45-49, 1980.

0819. EMORY UNIVERSITY, SCHOOL OF DENTISTRY, 1462 Clifton Road, NE., Atlanta, Georgia 30322.

Project Title:
Effects of Smokeless Tobacco on Periodontal Disease and Mucosal Health.

Principal Investigators:
Offenbacher, S.; Weathers, D.R.
Objective:
To (1) determine whether chronic smokeless tobacco (ST) use causes localized changes in human periodontal status as reflected in clinical assessments of inflammation (erythema, edema, suppuration, bleeding on probing, pain on probing, or attachment levels); (2) examine effects of chronic use on local subgingival microbial composition and relative numbers of crevicular polymorphonuclear leukocytes (PMNL) in humans; (3) assess relationship between local crevicular fluid concentrations of prostaglandin E_2 (PGE_2), a biochemical mediator of inflammation, and chronic use of tobacco products in humans; (4) evaluate effects of acquiring ST usage habit on the periodontium and other soft tissue and cellular composition; (5) examine human gingival biopsies from chronic ST users for possible histological changes in gingival epithelium, connective tissue, and cellular composition; and (6) evaluate a target population of adolescent male children to determine statistical parameters of prevalence, incidence, and frequency with regard to ST use and oral findings.
Methods or Approach:
Use of ST products, such as snuff and chewing tobacco, was investigated in a school population of 565 males (mean age 13.8 years). All students completed a tobacco usage questionnaire and were given intraoral examinations to determine possible relationships between ST use and presence of gingivitis, gingival recess, mucosal pathology, and caries. In microbiological studies, prevalence of darkfield morphotypes was examined. Ten different morphotypes were studied to determine prevalence, log number, and risk of acquisition. A definite tobacco usage/nonusage history was verified for 196 of 495 leukokeratoses. Histological features of cases were studied in a blinded evaluation, comparing findings in tobacco users and nonusers. PMNL were examined and enumerated in users

and nonusers at 286 periodontal sites. For determination of PGE_2 levels by radioimmunoassay, 502 crevicular fluid analyses were performed.

Results to Date:

The overall prevalence of ST usage was 13.3 percent compared with 1.4 percent for cigarette smoking, which indicates that the potential long-term health effects of ST use will be of increasing significance. In students with clean mouths that were free of gingivitis, the use of ST was not associated with a change in prevalence of gingival recession or mucosal pathology, or in mean DMF score (measure of dental caries based on numbers of decayed, missing, and filled teeth). In contrast, ST use was a significant risk factor in individuals with coexisting gingivitis, associated with a marked increase in prevalence of gingival recession, mucosal pathology (principally leukokeratoses), and caries experience. Data indicate that there are significant clinical and microbial changes that are attributable to ST use. Since none of the changes appear to occur in individuals with good oral hygiene, changes may first require a shift in microbial composition and clinical signs of inflammation. This hypothesis is supported by histological studies of leukokeratotic changes that showed that of the 196 cases, 90.3 percent were chronic tobacco users. This high prevalence of tobacco use in the leukokeratotic population might suggest an association between tobacco use and presence of leukokeratotic lesions. Although tobacco use was a significant risk factor for development of leukokeratoses, no single or multiple histological feature could be attributed to tobacco use and neither the degree of dysplasia nor the presence of frank carcinoma could be attributed to tobacco use. Data on PMNL showed that 49.4 percent of nonuser sites had detectable PMNL counts. This was not significantly different from ST users, who had PMNL at 44.1 percent of the sites. There was no evidence for increased PMNL egress into the periodontal pocket as a result of ST use. Detectable levels of PGE_2 were found in 123 subjects (24.5 percent), which is not significantly different from detection profiles of healthy individuals. The mean level is less than 10 ng PGE/mL crevicular fluid, a figure that indicates that the concentration of this important mediator of inflammation is lower than that associated with gingivitis and periodontitis patients (33.1 and 57.2 ng/mL, respectively). Activation of the ARA cascade, however, can lead to other extremely important metabolites, and modulation of this pathway may be important in ST-associated tissue changes.

Future Plans:

The scope of the microbiological investigations will be increased to include cultivable studies; effects of ST usage on progression of periodontal disease and mucosal health will be studied in the rhesus monkey; and the role of ST in the biochemistry of inflammation as it relates to periodontal disease and mucosal pathology will be investigated in humans and the rhesus monkey.

Project Dates:

July 1982–June 1985.

Financial Support:

Smokeless Tobacco Research Council, Inc.

0820. MOREHOUSE SCHOOL OF MEDICINE, Department of Microbiology and Immunology, 720 Westview Drive, SW., Atlanta, Georgia 30310.

Project Title:

Immune Cell Changes After Benzopyrene Insult In Utero.

Principal Investigator:

Urso, P.

Objective:

To determine the effects of prenatal insult of mice with benzo(*a*)pyrene (BaP) on (1) quantitative changes in T, B, and adherent (macrophage) cells in the insulted progeny; (2) the functional capacity of the cells on the growth of syngeneic and allogeneic tumors in vitro and in vivo (by Winn assay); (3) development of T cell subsets and their activity against syngeneic tumor during ontogeny and postnatal life; correlate activity of T cell subsets, B cells, and macrophages with tumorigenesis in progeny disposed toward a high incidence of tumors.

Methods or Approach:

Pregnant C3H/Anf mice are given a single i.p. injection of BaP of 150 μg/g body weight (about 3 μg enter the fetuses) and lymphoid tissue from the progeny are analyzed for changes in T cells, B cells, and macrophages during gestation and postnatally. Quantitative analysis of T cells and subsets ($Lyt\text{-}1^+$, $Lyt\text{-}2^+$) is accomplished with monoclonal antibodies $+C'$ using the trypan blue dye exclusion (TBDE) test. B cells are also quantitated with anti IgM $+C'$ with the TBDE test. Functional analyses of the cells and macrophages will be tested in MLR (T helpers, T suppressors) against syngeneic and allogeneic tumors by cytotoxicity for T cytotoxic cells and in ADCC for B cells and macrophages.

Results to Date:

Suppressed MLR and in vivo GVHR for lymphocytes of mouse progeny exposed to BaP have been shown. No difference was seen in cell numbers between BaP- and corn-oil-exposed progeny (15 to 19 days gestation). T cells of BaP-exposed progeny were reduced in fetal liver and spleen at 17 to 19 days. At 0 to 5 days postnatally, a marked depression in cell number occurred in the thymus, but there was a striking increase in the spleen. $Lyt\text{-}23^+$ cells were elevated in fetal liver and spleen at 17 days. In mothers, there was a severe reduction in T cells from gestation day 15 that persisted postnatally (0 to 5 days) in the thymus. The changes may explain the immunodeficiency of spleen cells from BaP-exposed progeny against syngeneic tumor, recently observed in a Winn assay. Findings suggest that BaP induces a disorientation of T cell differentiative pathways, resulting in disproportionate development of the T cell repertoire during ontogeny, a condition that may increase the sensitivity for neoplastic expression in progeny.

Future Plans:

Since an increase in $Lyt\text{-}2^+$ cells was observed, experiments are planned to determine the activity of these cells in terms of T suppressors or T cytotoxic cells. Changes in the mother during the gestational and early postnatal periods in T cells prompts an analysis of the activity of the subsets in the parent against syngeneic tumors. The activity of B cells and macrophages in the ADCC phenomenon will be measured. Additional plans include development and function of natural killer cells in the mother and progeny after gestational insult with BaP, analysis of T cell behavior in progeny exposed during midgestation, and comparison with those of progeny exposed in late gestation. The first show a higher frequency of ovarian tumors.

Project Dates:

September 1983–August 1987.

Financial Support:

NIH (5SO6 RR08006-14).

Reference:

Urso, P., Gengozian, N. "Alterations in the Humoral Immune Respose and Tumor Frequencies in Mice Exposed to Benzo(a)pyrene and X-Rays Before or After Birth." *Journal of Toxicology and Environmental Health* 10(4/5):817-835, October-November 1982.

0821. USDA, AGRICULTURAL RESEARCH SERVICE, RUSSELL RESEARCH CENTER, P.O. Box 5677, Athens, Georgia 30613.

Project Title:
Determination of Tobacco Leaf Precursors of Safety, Quality, and Host-Plant Resistance Factors.

Principal Investigators:
Severson, R.F.; Chortyk, O.T.

Objective:
To develop analytical methods to determine leaf components that are responsible for disease or insect resistance or are precursors of hazardous or flavor compounds of smoke; apply methods to evaluate selected samples.

Methods or Approach:
Quantitative methods will be developed to determine cured or green leaf sterols, lipids, terpenes, esters, polyphenols, alkaloids, carotenoids, sugar esters, carbonyls, etc., that may serve as precursors of hazardous tobacco smoke compounds (polycyclic aromatic hydrocarbons, phenols, amines, acids, or other biologically active compounds) or are precursors of flavor and aroma constituents (carbonyls, esters, furans, pyrazines, etc.). Compounds will be separated and identified by standard chromatographic and quantitative assays of newly developed germplasm or samples produced by different agronomic or curing methods to develop a safer tobacco. Green tobacco leaf will be evaluated for cuticular and internal components that may be involved in disease or insect resistance. Identified compounds will be properly tested and evaluated, and unavailable compounds will be isolated or synthesized.

Results to Date:
Tobaccos with high levels of diols were very susceptible to budworm damage, but tobaccos high in diols and sucrose esters were resistant. Cuticular labdanes and aliphatic hydrocarbons were not major factors in resistance. Thus, more than one type of tobacco leaf surface chemistry is responsible for budworm resistance. Budworm moth oviposition was stimulated by spraying a diol-containing solution onto a resistant diol-free tobacco. Tobaccos low in diols were resistant to aphids, but susceptible to flea beetles. A revised leaf wash procedure was developed. Methods were developed to analyze green tobacco budleaf for alkaloids, polyphenols, maleic and citric acids, sugars, and solanesol. Work is continuing on the isolation and characterization of the sucrose ester isomers. Wax esters have been shown to be comprised of C_{18}-C_{30} fatty alcohols bound to C_{12}-C_{30} fatty acids. Large quantities of surface chemicals have been isolated for spray-back studies to determine active constituents. Techniques have been developed for the laboratory preparation of glass capillary GC columns. Volatile fatty acids were analyzed on fused silica columns of SP-1000. The design, construction, and application of an open split interface for a capillary GC/MS was completed.

Future Plans:
Crosses of low solanesol with flue-cured tobaccos will be evaluated and inheritance patterns for sucrose esters will be determined. Cold on-column injection techniques will be developed.

Project Dates:
November 1982–November 1987.

Financial Support:
ARS.

0822. USDA, AGRICULTURAL RESEARCH SERVICE, RUSSELL RESEARCH CENTER, P.O. Box 5677, Athens, Georgia 30613.

Project Title:
Characterization of Hazardous and Quality Components of Tobacco Smoke.

Principal Investigators:
Snook, M.E.; Chamberlain, W.J.; Chortyk, O.T.

Objective:
To (1) identify health-related hazardous tobacco smoke compounds and flavor and aroma constituents; (2) develop analytical methods for isolation, identification, and quantitation of known or suspected tumorigenic or organoleptic compounds of tobacco smoke such as aza-arones, aliphatic and aromatic amines, nitrile compounds, nitro compounds, and nitrosamines; (3) analyze the weak acid, strong acid, and basic fractions of cigarette smoke condensate; (4) fractionate and analyze constituents of a tumor-inhibiting neutral smoke fraction to determine specific inhibitors; and (5) submit, as required, isolated compounds, fractions, or corresponding pyrolysis fractions for short-term bioassay studies.

Methods or Approach:
Volatile and particulate phases of cigarette or tobacco smoke will be separated and analyzed for toxic or tumorigenic smoke constituents, and weak acid, strong acid, and basic fractions of cigarette smoke will be analyzed. Methods of collection, fractionation, and analysis will be developed as required. The Ames bioassay will be developed and applied to isolated fractions and compounds. Trapping and GC-2 profile methods will be developed for flavor/aroma smoke compounds. Developed methods will be applied to evaluation of new germplasm or tobacco products to guide genetic-agronomic development of a safer tobacco that retains desired flavor/aroma characteristics.

Results to Date:
A universally applicable method for rapid and quantitative analysis of harman (H) and norharman (NH) was developed, using smoke trapping on Cambridge pads and analyses by GC-2. A linear relationship was found between tar levels of commercial and research cigarettes and levels of smoke H and NH. It was shown that H and NH production does not depend on alkaloid content of tobacco and that different tobacco types produced similar levels. Seventeen N′-acylalkaloids, mainly acylnornicotines, were determined, and three new ones were identified. Work was initiated on a method for amino-α-carboline, a potent mutagen of smoke. Work is progressing on characterizing the phenolic acids of smoke. N-nitrosonornicotine (NNN) was successfully determined in unburned tobacco by a GC-2 method. Application to numerous tobacco samples showed that there was no correlation between NNN levels and nicotine and nornicotine levels. Fused silica capillary GC columns of Silar 10C, prepared for the first time, were used to separate fatty acids by degree of unsaturation. Work is progressing on quantitation of tobacco-specific nitrosamines by selected ion monitoring mass spectrometry.

Future Plans:
A major fraction of smoke bases will be characterized and large ring aza-arenes will be quantitated. Polyphenols will be determined and phenolic acids of smoke will be identified. Methods for the reduction of NNN will be studied.

Project Dates:
December 1982–November 1987.

Financial Support:
ARS.

0823. UNIVERSITY OF GEORGIA, COASTAL PLAIN EXPERIMENT STATION, Tifton, Georgia 31793-0748.

Project Title:
Chemical Analysis of Experimental Flue-Cured Tobacco.

Principal Investigator:
Gaines, T.P.
Objective:
To investigate and determine the effects of various agronomic, varietal, physiological, curing, engineering, entomological, and pathological experiments on the chemical quality constituents of flue-cured tobacco from field and greenhouse studies conducted by the University of Georgia Tobacco Research and Extension staffs.
Methods or Approach:
Experimental flue-cured tobacco samples were analyzed for the following chemical quality constituents: total alkaloids, nicotine, nornicotine, total nitrogen, protein nitrogen, nitrate nitrogen, total reducing sugars, starch, total nonstructural carbohydrates, total ash, alkalinity of water-soluble ash, potassium, calcium, phosphorus, chlorine, and sulfur.
Results to Date:
Chemical constituents of tobacco can be altered each year by cultural practices, varieties, stalk position, fertilizer, curing, plant growth regulators, soil type, and weather to produce tobacco with predetermined chemical composition.
Project Dates:
1962–continuing.
Financial Support:
Georgia Agricultural Commodity Commission for Tobacco (25-21-RF328-211); University of Georgia.

0824. UNIVERSITY OF GEORGIA, COASTAL PLAIN EXPERIMENT STATION, Tifton, Georgia 31793.

Project Title:
Investigations of Soil-Borne Diseases of Tobacco.

Principal Investigator:
Csinos, A.S.
Objective:
To investigate methods for controlling soilborne diseases of tobacco, including black shank, *Sclerotium rolfsii*, and nematodes.
Methods or Approach:
Randomized replicated plots will be established in disease nurseries and treatments (chemical, cultural, or application technology) will be evaluated.
Results to Date:
Soilborne diseases can be significantly decreased with application of pesticides if cultivars with resistance are incorporated. Date of planting affects severity of diseases; later plantings have reduced disease. Chemicals applied through irrigation water are as efficacious as conventionally applied chemicals.
Future Plans:
The use of new application technologies will be continued to investigate reduced rates of pesticide use, and new chemical fungicides will be evaluated for black shank control.
Project Dates:
August 1978–August 1988.
Financial Support:
University of Georgia; Georgia Agricultural Commodity Commission for Tobacco; R.J. Reynolds, Inc.

0825. UNIVERSITY OF GEORGIA, ATHENS, Department of Biochemistry, Athens, Georgia 30602.

Project Title:
Pulmonary Emphysema and Proteolysis.

Principal Investigator:
Travis, J.
Objective:
To determine events that lead to development of pulmonary emphysema.
Methods or Approach:
The final stages of emphysema involve the degradation of connective tissue proteins of the lung and, therefore, involve proteolysis. It is the lack of control of the proteolytic enzymes that are of concern and the inactivation of inhibitors of proteolysis by oxidative components created either indirectly or directly by smoke that appears to be a key to emphysema development. Properties of the α_1-proteinase inhibitor plasma protein, which controls elastolysis in the lung, are being investigated to determine how oxidation affects activity of this inhibitor.
Results to Date:
Data indicate that oxidation of the reactive site methionine of α_1-proteinase inhibitor markedly reduces its ability to inactivate neutrophil elastase. The reduction in association rate allows the enzyme to compete for elastin and, thereby, increases the rate of degradation of connective tissue components. It has been shown that by using a recombinant DNA mutant in which the reactive site methionine has been altered to valine, the inhibitor can no longer be oxidatively inactivated. The source of the oxidant is undoubtedly myeloperoxidase derived from neutrophils invading the lung tissue, while a secondary source may be that obtained directly from cigarette smoke.
Future Plans:
The effect of further modification of the reactive site of α_1-proteinase inhibitor will be assessed to determine the potential use of recombinant DNA-derived proteins for therapy and to investigate how enzymes that reduce oxidation might be used in treating various forms of attack on the lung.
Project Dates:
January 1982–December 1987.
Financial Support:
NHLBI.

0826. USDA, ARS, GEORGIA COASTAL PLAIN EXPERIMENTAL STATION, Tifton, Georgia 31794.

Project Title:
Cultural and Nutritional Studies in Tobacco Production.

Principal Investigator:
Stephenson, M.G.
Objective:
To conduct cultural and nutritional studies in tobacco production.
Methods or Approach:
Three methods, using two materials (Budnip PPG575 and Prime Plus, Ciba-Geigy) were used to determine sucker control, yield, and quality results at this location. Methods in advanced regional sucker control test were FA/Prime Plus, (4 percent + 9/mg, respectively) in two applications, FA/Prime Plus (4 percent + 9/mg) in a single application, and FA/BN/BN (4 percent/85 mg) in three applications. Over 650 breeding lines, crosses, and cultivars were screened under field conditions to identify insect resistant germplasm. Alkaloid and N-nitrosonornicotine (NNN) contents of various tobaccos

were also determined. Effect of nitrogen fertilization on NNN production was evaluated by growing a normal flue-cured tobacco (NC2326) and a converter tobacco (NIC117H-1) at three different levels of nitrogen fertilization.

Results to Date:
The three methods for sucker control had good results in control and in tobacco yield and quality. Four multiple disease resistant varieties (Coker 82-211Y, NK2117, PD279, and VA102) were declared eligible for variety release by the regional flue-cured tobacco evaluation committee. NC2326 showed a significant increase in NNN levels with increased rate of nitrogen fertilization. A 76 percent reduction in amount of NNN was achieved by spraying freshly harvested leaf with either ascorbic acid or alpha-tocopherol solution.

Financial Support:
USDA (Geo-02-0214).

References:
Arnett, S.C.; Csinos, A.S.; Stephenson, M.G., et al. *1984 Georgia Tobacco Research and Extension Report.* Georgia College of Agriculture Miscellaneous Publication No. 106, 1984. (2) Gaines, T.P.; Stephenson, M.G. "Determining the Sulfur to Nitrogen Requirement of Flue-Cured Tobacco. *Tobacco Science* 28:91-92, 1984. (3) Seltmann, H.; Priest, J.S.; Stephenson, M.G., et al. *Regional Tobacco Regulator Tests Flue-Cured.* USDA, ARS, January 1984 (4) Severson, R.F.; Arrendale, O.T.; Stephenson, M.G., et al. "Quantitative Methodology of the Cuticular Components of Green Tobacco." *Journal of Agriculture and Food Chemistry* 32(3);556-570, June 1984. (5) Stephenson, M.G. "Clipping Effects on Transplant Yield and Field Performance of Flue-Cured Tobacco." *Tobacco Science* 28:55-58, 1984. (6) Stephenson, M.G. *1984 Flue-Cured Variety Test: Field Crops Performance Test.* University of Georgia, College of Agriculture Research Report, January 1985.

0827. VETERANS ADMINISTRATION, 2460 Wrightsboro Road, Augusta, Georgia 30910.

Project Title:
Effects of Carcinogens on Macromolecular Events in the Pancreas.

Principal Investigator:
Black, O., Jr.

Objective:
To study certain nuclear processes in pancreatic tissue following the administration of carcinogens that are known inducers of pancreatic tumors; examine the hypothesis that, as in other tissues, interaction of carcinogens with nuclear components occurs in the pancreas, resulting in altered regulatory and synthetic processes that could eventually lead to pancreatic tumor formation.

Methods or Approach:
The effects of the carcinogen 3,4-benzo(*a*) pyrene on ornithine decarboxylase enzyme activity in pancreatic tissue were examined.

Results to Date:
The carcinogen caused three transient elevations in enzyme activity of 2, 16, and 36 hours posttreatment. These changes corresponded to other macromolecular events in the pancreas, a change in DNA content at 2 hours, a change in content at 16 hours, and a significant rise in RNA content at 36 hours. These studies confirm other observations from the literature relating to carcinogen-induced changes in ornithine decarboxylase enzyme levels.

Financial Support:
VA.

Hawaii

0828. KAUKINI MEDICAL CENTER, 347 North Kaukini Street, Honolulu, Hawaii 96817.

Project Title:
Honolulu Heart Program (HHP).

Principal Investigator:
Yano, K.

Objective:
To investigate incidence of and mortality from coronary heart disease (CHD) and stroke and risk factors among men of Japanese ancestry who were born between 1900 and 1919 and lived on Oahu Island, Hawaii in 1965.

Methods or Approach:
Based on World War II Selective Service Registration, over 11,000 men of Japanese ancestry who were born on Oahu Island and lived there in 1965 were identified and located. Of these men, 8,006 participated in initial examinations (1965 to 1968) that included detailed interviews to obtain information on social and medical history and living habits, including smoking, alcohol consumption, diet, and physical activity. Body measurements, blood pressure determinations, and physical examination focused on the cardiovascular system. Laboratory study included urinalysis, blood chemistry, timed vital capacity, and 12-lead resting electrocardiogram. Disease endpoints (CHD, stroke, and all deaths) have been ascertained by reexaminations and by comprehensive surveillance of morbidity and mortality based on hospital records, death certificates, and autopsy reports.

Results to Date:
Prevalence, incidence, and mortality rates of CHD were significantly higher in the HHP cohort than in a comparable cohort in Japan. In contrast, rates for stroke were only one-third the rates among the Japanese cohort. Findings were confirmed by autopsy studies. CHD incidence was less than half that of Caucasian populations in the United States. Multivariate analysis of 10-year followup data showed the most significant risk factors for CHD to be high blood pressure and cigarette smoking. Serum cholesterol and glucose intolerance were also important risk factors. Moderate consumption of alcohol and carbohydrate intake were protective factors for CHD. High blood pressure was the strongest risk factor for stroke. Age and cigarette smoking also significantly increased the risk of hemorrhagic and thromboembolic strokes. Glucose intolerance and proteinuria were risk factors only for thromboembolic stroke, while serum uric acid and serum cholesterol (inversely) were risk factors only for hemorrhagic stroke. ECG evidence of LVH significantly increased risk of theomboembolic stroke and cerebral hemorrhage, but not of subarachnoid hemorrhage.

Future Plans:
Morbidity, mortality, and autopsy surveillance of the cohort will continue. In addition, the relationship of pulmonary function to biological and lifestyle variables, respiratory symp-

toms, and cardiovascular morbidity and mortality will be studied.
Project Dates:
October 1965–June 1990.
Financial Support:
NHLBI (HC-85-3).

0829. UNIVERSITY OF HAWAII, 1960 East-West Road, Honolulu, Hawaii 96822.

Project Title:
Urothelial Cancer in Hawaii.

Principal Investigator:
Nomura, A.M.
Objective:
To investigate association of urothelial cancer with coffee, artificial sweeteners, hair dye, vitamin A and vitamin C, smoking, and occupation in two ethnically distinct groups that have different levels of risk.
Methods or Approach:
All initially diagnosed cases on the Hawaiian island of Oahu during the study period will be identified, and two controls for each case, from the general population and matched for sex, race, and age (within 3 years), will be identified and interviewed. The questionnaire and study format are similar in design to an ongoing case–control study being conducted by the Harvard School of Public Health in three different populations (including Japanese in Nagoya, Japan, who are at low risk). Findings will be compared between the Japanese in Hawaii and Nagoya, and between Caucasians and Japanese in Hawaii to identify factors that may contribute to the differences in risk between the respective groups.
Results to Date:
Results are not yet available.
Financial Support:
NCI (5R26CA25903-03).

0830. UNIVERSITY OF HAWAII, MANOA, CANCER CENTER OF HAWAII, 1236 Lauhala Street, Honolulu, Hawaii 96813.

Project Title:
50,000 Member Cohort Study of Alcohol and Cancer.

Principal Investigators:
Hinds, M.W.; Kolonel, L.N.; Lee, J.H., et al.
Objective:
To examine the risk of site-specific cancer in relation to history of alcohol intake.
Methods or Approach:
Approximately 50,000 adult residents were interviewed from 1975 to 1980 for their quantitative and beverage-specific alcohol use. Smoking history, height, weight, age, sex, and race were also determined. These subjects have been matched to the statewide Hawaii Tumor Registry records to identify those who developed cancer post-interview. Multivariate statistical methods will be used to determine the site-specific cancer risk associated with various levels of alcohol consumption and consumption of different beverages while adjusting for smoking, age, sex, and race.
Results to Date:
Results are not yet available.
Project Dates:
September 1981–1983.
Financial Support:
NCI (R01-CA30119).

0831. UNIVERSITY OF HAWAII, MANOA, CANCER CENTER OF HAWAII, 1236 Lauhala Street, Honolulu, Hawaii 96813.

Project Title:
Health Effects of Asbestos Exposure Among Pearl Harbor Naval Shipyard Workers.

Principal Investigator:
Kolonel, L.N.
Objective:
To assess the cancer risk among workers exposed to asbestos in a naval shipyard.
Methods or Approach:
A cohort of nearly 9,000 shipyard workers employed during the period 1950-1970 was classified in terms of likely exposure or nonexposure to asbestos based on work histories. In addition, smoking histories were obtained on those men alive and residing in Hawaii during 1977. Surveillance is being carried out on the entire cohort for cancer incidence and mortality. Prospective followup will permit assessment of the interaction between smoking and asbestos.
Results to Date:
A mortality analysis using the modified life-table method showed an increased risk of lung cancer (relative risk = 1.7) in the exposed group after 20-24 years of observation, compared with the general population of Hawaii (matched for age, sex, ethnicity, and calendar period of observation). A similar analysis of the nonexposed group showed no increased risk for lung cancer.
Future Plans:
Continued surveillance will be done on the total cohort. A mortality analysis based on an additional 5 years of followup is in progress. Prospective followup on the group with smoking histories is planned. Cancer incidence will be determined through the local statewide tumor registry.
Project Dates:
June 1976–continuing.
Financial Support:
USN (N-00014-76-C-0952).

0832. UNIVERSITY OF HAWAII, MANOA, CANCER CENTER OF HAWAII, 1236 Lauhala Street, Honolulu, Hawaii 96813.

Project Title:
Case–Control Study of Lung Cancer and Dietary Vitamin A in Hawaii.

Principal Investigators:
Hinds, M.W.; Kolonel, L.N.; Nomura, A.M., et al.
Objective:
To investigate the relationship between risk of lung cancer at several levels of smoking and dietary intake of vitamin A and vitamin A precursors.
Methods or Approach:
Over a period of 3 years, 364 lung cancer patients and 627 age- and sex-matched neighborhood controls were interviewed. Men and women of Caucasian, Japanese, Chinese, Philippine and Hawaiian/part-Hawaiian ethnic groups were included. Trained interviewers administered a questionnaire in the homes of cases and controls. The questionnaire included both frequency and quantitative information on approximately 84 dietary items as well as smoking and occupational histories. The dietary items were chosen to account for at least 85 percent of vitamin A intake for each ethnic group based on previously collected 3-day diet records.

Results to Date:
After adjusting for a number of potentially confounding variables, including ethnicity, smoking history, and occupation, evidence was found that total vitamin A intake, vitamin A intake from food sources only, and carotene intake were each inversely associated with lung cancer risk in males, but not in females.
Future Plans:
An extension of the study, in which additional cases and controls are being interviewed, will examine the association of vitamin A intake with specific histologic types of lung cancer in men and women.
Project Dates:
August 1979–continuing.
Financial Support:
NCI (R01-CA26515).

0833. UNIVERSITY OF HAWAII, MANOA, CANCER CENTER OF HAWAII, 1236 Lauhala Street, Honolulu, Hawaii 96813.

Project Title:
Epidemiologic Survey of Hawaii Residents.
Principal Investigators:
Kolonel, L.N.; Nomura, A.M.; Hinds, M.W., et al.
Objective:
To determine the relationship between health habits and demographics in Hawaii; relate this information to cancer incidence and mortality among the various ethnic groups in Hawaii.
Methods or Approach:
In 1975, a brief epidemiological questionnaire was added to the on-going Health Survey of Hawaii, a statewide survey patterned after the U.S. National Health Survey. About 6,000 households are surveyed annually, and the epidemiological questionnaire was administered for a period of years, yielding a sample of nearly 50,000 subjects. The questionnaire included information on smoking, drinking, and dietary habits as well as various demographic data (age, sex, race, place of residence, education, and income).
Results to Date:
The cohort developed through the survey will be followed prospectively for cancer risks in relation to antecedent dietary and smoking habits.
Project Dates:
1975–continuing.
Financial Support:
NCI.

Idaho

0834. VETERANS ADMINISTRATION MEDICAL CENTER, Clinical Pharmacology and Gerontology Unit, 500 West Fort Street, Boise, Idaho 83702.

Project Title:
Geriatric Clinical Pharmacology of Methylxanthines.

Principal Investigator:
Vestal, R.E.
Objective:
To (1) increase understanding of the pharmacological interactions of drugs and environmental compounds with theophylline, a methylxanthine compound related to caffeine (used in acute and chronic management of patients with asthma and chronic obstructive pulmonary disease (COPD), but which can cause clinical toxicity at elevated plasma levels); (2) provide basis for safe and effective use of theophylline by examining effect of age and cigarette smoking on inhibition and induction of theophylline metabolism; and (3) investigate the general hypothesis that the adaptive response of the human liver is altered by aging.
Methods or Approach:
Phase 1 will investigate inhibition of theophylline metabolism by cimetidine in 20 healthy male volunteers in two age groups: 18 to 40 years and over 65 years of age. Half of the subjects in each group will be cigarette smokers (>20 cigarettes/day) and half will be nonsmokers. Disposition of theophylline will be determined after single dose i.v. administration before and after coadministration of cimetidine (1,200 mg/day x 7 days). Plasma theophylline and cimetidine will be determined by high performance liquid chromatography. Urinary theophylline and its metabolites will be determined by a newly developed capillary gas chromatography/mass spectrometry method. Plasma protein binding, plasma thiocyanate, and urinary 6β-hydroxycortisol and d-glucaric acid will also be determined. Phase 2 will investigate induction of theophylline metabolism by phenytoin in a similar group of subjects, using a similar protocol.
Results to Date:
In a preliminary study, inhibition of theophylline metabolism by cimetidine was investigated in six young male cigarette smokers and six nonsmokers by stable isotope methodology. Theophylline bioavailability, volume of distribution, and protein binding were of the same order in both groups and were not affected by cimetidine. Plasma thiocyanate concentrations were higher in smokers than in nonsmokers and were related to theophylline clearance. Findings indicate that cimetidine inhibits theophylline metabolism to a similar extent in young smokers and in young nonsmokers. Determination of plasma thiocyanate levels may be valuable in prediction of theophylline clearance.
Future Plans:
Using theophylline as a model compound and clinically relevant therapeutic drug, study results will provide data to evaluate effect of age and cigarette smoking on adaptive response of the human liver to microsomal enzyme inhibition and induction.
Project Dates:
September 1984–August 1987.
Financial Support:
NIA (AG 02901).
Reference:
Cusack, B.J.; Dawson, G.W.; Mercer, G.D., et al. "Cigarette Smoking and Theophylline Metabolism: Effects of Cimetidine." *Clinical Pharmacology and Therapeutics* (In press).

0835. AMERICAN LUNG ASSOCIATION OF DUPAGE AND MCHENRY COUNTIES, 526 Crescent Boulevard, Glen Ellyn, Illinois 60137.

Project Title:
Biofeedback Smoking Education (BIOSEP).

Principal Investigator:
Wimmer, H.
Objective:
To evaluate the Biofeedback Smoking Education Program (BIOSEP).
Methods or Approach:
BIOSEP is based on the concept that changes in attitudes and behaviors will occur when students see the immediate physiological changes that take place in the body after only one cigarette. The program also offers nonsmokers a chance to reinforce the decision not to smoke by comparing results with those of smokers. Biofeedback machines and a biological demonstration test are the major program components. The machines used, which enable students to individually pursue the knowledge needed to make an objective decision about smoking, include (1) pulse rate monitor (measures physiological response to tobacco); (2) digital thermometer (measures skin temperature of the hands); (3) tremor tester (measures hand tremor); and (4) carbon monoxide analyzer (measures carbon monoxide level in expired air). Data will be collected on smokers before and after smoking a cigarette (parental permission is required).
Results to Date:
Results to date show that among smokers, 20.4 percent of the students stopped smoking after participation in the program and 47.7 percent stated that the program influenced attitudes toward smoking. Among nonsmokers, 88.4 percent stated that the decision not to become a smoker was reinforced. Among all participants, 91.5 percent said they would recommend the program to friends.
Project Dates:
September 1984–continuing.
Financial Support:
ALA, DuPage and McHenry Counties.

0836. CARLE CLINIC ASSOCIATION WELLNESS CENTER, 602 West University, Urbana, Illinois 61820.

Project Title:
Long-Term Followup of Smoking Cessation Participants in the Stop Smoking Clinic of the Carle Wellness Center.

Principal Investigator:
Morrison, S.A.
Objective:
To (1) compare long-term cessation rates of participants with national statistics; (2) recognize common reasons for failure; (3) adapt program to better meet needs of participants; and (4) determine effectiveness of gradual withdrawal (Wellness Center method) as opposed to other available methods.
Methods or Approach:
Mail and telephone surveys, conducted on a 3-month and yearly basis, determine participant's current smoking behavior compared with behavior at the end of the clinic program. Data will be compared by sex, age, occupation, years smoked, amount smoked, and reasons for current smoking behavior.
Results to Date:
Although data show a considerable degree of variation between classes, abstinence in all classes remains above the national average success rate.
Future Plans:
As national trends shift to a smokeless society, the methods used in the ongoing project to help smokers quit will be reevaluated and improved.
Project Dates:
July 1984–July 1985.
Financial Support:
Carle Clinic Association Wellness Center.

0837. NORTHWESTERN MEMORIAL HOSPITAL, 259 East Erie, No. 103, Chicago, Illinois 60626.

Project Title:
Physiologic Influences on Sodium-Lithium Transport (Human).

Principal Investigator:
Ostrow, D.G.
Objective:
To assess physiologic factors affecting sodium-lithium transport measurements in a population determined to be free of psychiatric illness.
Methods or Approach:
Primary factors of interest are age, sex, race, blood pressure, hypertension, body mass, and alcohol intake. Secondary variables of interest include family history of hypertension, family history of psychiatric illness, differences between pre- and postmenopausal females, tobacco intake, major medical illness, and medication. Four hundred volunteers will be recruited from a private health screening facility and selected for absence of major psychiatric illness using the Diagnostic Interview Schedule. The importance of family psychiatric history will be assessed with the Research Diagnostic Criteria for Family History. Blood samples will be taken for lithium efflux determination. The project offers a thorough assessment of physical characteristics affecting lithium transport, which must be the necessary next step for application of this measurement to large-scale studies of biological markers in pyschiatric illness.
Results to Date:
Earlier observations were made of effects of hypertension, blood pressure, body mass, sex, and race on lithium efflux in an affectively ill population, but there have been no studies of a large group of nonpsychiatric patients carefully screened for a wide range of medical variables. Lithium efflux was increased in essential hypertension, emphasizing the need to fully understand the effects of physiologic variables on this measurement before it can be applied to diagnostic studies.
Financial Support:
NIMH (1R01MH37930-01).

0838. NORTHWESTERN UNIVERSITY MEDICAL SCHOOL, Department of Pathology, 303 East Chicago Avenue, Chicago, Illinois 60611.

Project Title:
Hemoprotein-Catalyzed Oxygenations of Carcinogens.

Principal Investigator:
Hollenberg, P.F.

Objective:
To (1) develop an understanding of the mechanisms by which the liver microsomal cytochrome P-450-dependent mixed function oxidases catalyze the metabolic activation and detoxification of chemical carcinogens such as benzo(*a*)pyrene; (2) investigate the role of the components of the microsomal membrane in modulating the activity of these enzymes; and (3) study the inactivation of these enzymes by mechanism-based inactivators.

Methods or Approach:
The specific aims of this project are to investigate the steady-state kinetics of cytochrome P-450-catalyzed dealkylation reactions supported by a number of different peroxides and hydroperoxides to determine the kinetic mechanism(s) for the reactions. Several different purified isozymes of P-450 will be used to investigate the possibility that different forms of the enzyme may utilize different mechanisms to catalyze the same reaction. The effects of phospholipids on the kinetics of the peroxide-supported reactions will also be investigated. The substrate kinetic isotope effects on the P-450-catalyzed O-demethylation reactions supported by hydroperoxides and peroxides will be investigated to elucidate the chemical mechanism(s) by which the enzymes catalyze dealkylations. Substrate kinetic isotope effects and metabolic switching in P-450-catalyzed reactions, supported by NADPH and O_2, will be studied to gain a better understanding of the nature of the intermediates formed during catalysis. Reactions to be investigated are the O-deethylation of 7-ethoxycoumarin and the hydroxylation of N-nitroso-2,6-dimethylmorpholine. The substrate binding properties of the active site of cytochrome P-450 LM_2 wil be characterized and polypeptide sequences that are involved in forming the substrate site will be identified, using photoaffinity labeling of the active site. An investigation will be made of the suicide inactivation of cytochrome P-450b during metabolism of N-methylcarbazole, and the amino acid residue(s) and peptides(s) at the active site that are modified during inactivation will be identified.

Results to Date:
Steady-state kinetics of the chloroperoxidase- and horseradish peroxidase-catalyzed N-methylation of N,N-dimethylaniline showed that both enzymes catalyzed the reaction via a ping-pong BiBi mechanism. Studies on the intramolecular isotope effects for demethylation of N,N-dimethylaniline demonstrated that chloroperoxidase and the P-450-type cytochromes catalyze the reaction by a chemical mechanism involving oxidation of the amine to the anilinium ion followed by deprotonation, whereas the mechanism for proteins such as horseradish peroxidase, lactoperoxidase, hemoglobin, and myoglobin involves an initial hydrogen atom abstraction. The oxygen atom incorporated into product in cytochrome P-450-catalyzed demethylations was shown to be derived from the oxidant and not from the medium. The initial metabolism of N-nitroso-2,6-dimethylmorpholine, a potent pancreatic carcinogen, by cytochrome P-450, was studied and the difference between the carcinogenic potency of the cis and trans isomers was shown to be due to differences in routes of metabolism of these compounds, with the initial differentiation occurring at the level of cytochrome P-450. N-methylcarbazole was shown to be a suicide substrate for cytochrome P-450 that converted it from a hydroxylase to an oxidase.

Future Plans:
Further characterization will be made of (1) regulation of catalytic activity of microsomal mixed-function oxidases; (2) interactions of components of endoplasmic reticulum and effects of these interactions on catalytic activity of cytochrome P-450; (3) mechanism of action of P-450-type cytochromes; (4) active site of cytochrome P-450; and (5) role of this enzyme system in chemical carcinogenesis.

Project Dates:
September 1984–February 1988.

Financial Support:
NCI (RO1-CA-16954-09).

0839. NORTHWESTERN UNIVERSITY, TECHNOLOGICAL INSTITUTE, Evanston, Illinois 60201.

Project Title:
Arterial Wall Oxygen Transport System: Role in Atherosclerosis Etiology.

Principal Investigator:
Goldstick, T.K.

Objective:
To estimate the degree of carbon monoxide-induced arterial wall hypoxia associated with cigarette smoking; determine the potential that this hypoxia has for contributing to the development of atherosclerosis.

Methods or Approach:
Carbon monoxide acts both by inducing hypoxemia and by shifting the oxyhemoglobin equilibrium curve, with these effects acting on the oxygen transport system from both the luminal blood and the vasa vasorum. This system is studied using a computer simulation of the human arterial wall with various levels of blood carbon monoxide (CO) imposed on it.

Results to Date:
The computer simulation study indicates that significant, midmedial hypoxia with the blood CO levels are routinely found in smokers. Because these levels fluctuate, the hypoxia they induce would be expected to be uncompensated by increased vascularization, and could potentially represent a much more significant factor in atherogenesis than chronic hypoxia alone. Results of the computer simulation should be verified by measuring tissue pO_2 at various levels of blood CO in the wall tissue of the dog thoracic aorta. For this study, specially constructed oxygen microelectrodes could be passed slowly through the wall and the oxygen profile measured.

Project Dates:
January 1982–1983.

0840. NORTHWESTERN UNIVERSITY, TECHNOLOGICAL INSTITUTE, 2145 Sheridan Road, Evanston, Illinois 60201.

Project Title:
Use of Acoustic Energy to Study Pulmonary Systems.

Principal Investigator:
Jacobs, J.E.

Objective:
To determine the acoustic transmission of the pulmonary system as an indication of the changes in the system.

Methods or Approach:
The procedure involves introducing wide-band acoustic energy into the mouth of the individual. The energy transmitted is detected at various locations on the body by a series of microphones. The technique of cross-correlation is utilized to obtain the impulse response of the intervening pulmonary system. The impulse response is then utilized to obtain the frequency and phase characteristics of the transmitted acoustic energy. The amplitude and phase characteristics of the acoustic energy transmitted as a function of frequency may be used to determine the mechanical properties and hence the condition of the pulmonary system.

Results to Date:
Smokers and nonsmokers have been identified based on the acoustic transmission. Results to date indicate that the acoustic transmission of the pulmonary system is capable of delineating various types of small airways disease. A phenomenological model has been developed to account for some of the observed characteristics.

Future Plans:
Future work will be conducted to further expand the model and, coupled with data obtained in the clinic, identify the sources of the acoustic absorption obtained.

Project Dates:
August 1980–1983.

Financial Support:
Northwestern University; NIH (5 R01 HL25787).

Reference:
Jacobs, J. E. "Wideband Acoustic Energy Studies of Pulmonary Airways." *Journal of the Bioelectromagnetics Society* 3(1):167-177, 1982.

0841. NORTHWESTERN UNIVERSITY, Department of Pathology, 303 East Chicago Avenue, Chicago, Illinois 60611.

Project Title:
Sequential Analysis of Oral Carcinogenesis.

Principal Investigators:
Solt, D.B.; Calderon-Solt, L.

Objective:
To determine whether gamma-glutamyltranspeptidase (GGT) is expressed during development of squamous cell carcinoma of the oral cavity and contiguous structures; determine whether GGT expression is related to known oral cancer risk factors such as aging, tobacco use, alcohol intake, and prior neoplastic disease of the upper aerodigestive tract.

Methods or Approach:
Frozen sections are prepared from samples of carcinoma, dysplasia, and grossly uninvolved oral mucosa obtained from autopsy or surgery specimens. Sections are stained for GGT activity and evaluated in relation to known oral cancer risk factors of patients as documented in hospital records.

Results to Date:
Specimens of oral, pharyngeal, and laryngeal mucosa obtained from 46 patients have been evaluated for GGT histochemical activity. Generalized or patchy GGT activity has been observed in each of 26 squamous cell carcinomas and 33 dysplastic samples and in a single squamous papilloma. In addition, several samples of nondysplastic epithelium obtained from tobacco users displayed GGT activity.

Future Plans:
GGT biochemical assays will be used to quantitate expression of this enzyme in oral mucosa. Emphasis will be placed on expression of GGT in mucosal samples obtained from high-risk and low-risk elderly individuals to determine whether GGT expression is a function of aging, independent of known risk factors.

Project Dates:
July 1983–December 1986.

Financial Support:
NCI (R01CA34160); Smokeless Tobacco Research Council, Inc.

0842. SOUTH SUBURBAN HOSPITAL, 17800 South Kedzie Avenue, Hazel Crest, Illinois 60429.

Project Title:
Effect of Nicotine on Main and Digital Vessels.

Principal Investigators:
Adiga, K.R.; Doherty, S.J.

Objective:
To assess effects of nicotine on main and digital vessel hemodynamics by transcutaneous pO_2 measurements, volume pulse recordings, and photoplethysmography in chronic cigarette smokers with and without known peripheral arterial insufficiency.

Methods or Approach:
Measurements of oxygen tension and recordings of blood volume changes will be obtained before, during, and after smoking to determine the overall effect of nicotine on main and digital vessels in 60 subjects divided into three groups: (1) smokers with normal arterial hemodynamics, (2) smokers with known peripheral arterial insufficiency, and (3) smokers with known peripheral arterial insufficiency who have undergone reconstructive vascular procedures. A smoker is defined as a person with a 5-year history of smoking one or more packs of cigarettes/day. All participants will be 20 years of age or older.

Results to Date:
Results are not yet available.

Project Dates:
May 1982–May 1986.

Financial Support:
South Suburban Hospital, Illinois.

0843. SOUTHERN ILLINOIS UNIVERSITY, SCHOOL OF LAW, Carbondale, Illinois 62910.

Project Title:
Legal Aspects of Cigarettes and Fire Safety.

Principal Investigator:
Garner, D.W.

Objective:
To set forth the legal rights and liabilities that arise when a cigarette is involved in a fire and describe the factual and legal grounds to support an action against a cigarette manufacturer for the consequences of the cigarette-induced fire.

Methods or Approach:
A thorough search of the current literature on fires caused by cigarettes and means to make cigarettes safer was undertaken. In addition, an examination of the legal precedents and theories that can be applied to a cigarette fire situation were explored.

Results to Date:
Cigarettes are needlessly dangerous to users and those around them because they are not designed to minimize the risk of fire. Changes in the way cigarettes are designed, fabricated, and treated could result in fewer deaths, injuries, and property destruction. The law of product liability seeks to encourage product manufacturers to produce a product that is as safe as possible and also seeks to compensate plaintiffs who are needlessly injured. Both product safety and compensation of innocent victims can be accomplished by using current legal theory and practice to hold cigarette manufacturers liable for failure to take into account the safety of users and bystanders in the design of their product as it relates to fire danger.

Future Plans:
Publication of the legal theories is anticipated to support litigation in favor of fire victims against cigarette manufacturers.

Project Dates:
September 1983–March 1984.

0844. SOUTHERN ILLINOIS UNIVERSITY, Department of Health Education, Carbondale, Illinois 62901.

Project Title:
Smokeless Tobacco: Incidence of Use and Attitudes Toward Users in a University Population.

Principal Investigator:
McDermott, R.J.
Objective:
To (1) determine prevalence and psychosocial correlates of smokeless tobacco use in an undergraduate university population in the midwest; (2) identify attitudes of university undergraduates toward smokeless tobacco use; and (3) delineate beliefs concerning health-related outcomes of smokeless tobacco use.
Methods or Approach:
A modified version of the Marty-Williams Smokeless Tobacco Users Inventory was employed and administered to approximately 1,100 undergraduate students enrolled in general education classes during December 1984. The 25-item instrument sought data on prevalence, initiation, and reinforcement factors in smokeless tobacco use; prevalence of cigarette smoking among smokeless tobacco users; attitudes toward smokeless tobacco use; knowledge of health-related outcomes pertinent to smokeless tobacco; and selected demographic variables. Data will be analyzed using the *Statistical Package for the Social Sciences* (10th edition).
Results to Date:
Preliminary data indicate that smokeless tobacco use is virtually an exclusive male behavior and that social support initiates with a friend's influence.
Future Plans:
Knowledge, attitudes, behaviors, and psychosocial correlates of use among high school and elementary school students in the same geographic area will be examined.
Project Dates:
December 1984–May 1986.
Financial Support:
Southern Illinois University.

0845. SOUTHERN ILLINOIS UNIVERSITY, Department of Health Education, Lingle Hall 128, Carbondale, Illinois 62901.

Project Title:
Cigarette Advertisements in *Time* Magazine 1944-1983: A Content Analysis.

Principal Investigator:
Sofalvi, A.J.
Objective:
To analyze content of cigarette advertisements for health claims and health images.
Methods or Approach:
Health claims were defined as any slogans or statements that made a particular cigarette appear as if it could improve health or appear safer than a nontobacco substance, or that tried to minimize anxieties about the risks of smoking in general or in smoking a particular brand. Health images are those that implied that smoking is compatible with vitality, physical stress, and athletic activity; statements that are contradicted by medical evidence. It was expected that health images would be found more often than health claims after 1964, the year the first Surgeon General's Report on Smoking and Health was published. It was expected that health images would become prevalent as cigarette manufacturers attempted to counteract reports on smoking and illness by associating smoking with a healthy lifestyle. Each issue of *Time* from 1944 to 1983 was assigned a number and the sample was selected through a random numbers table. Issues were examined in chronological order. Totals and percentages of health claims and health images were calculated.
Results to Date:
A total of 527 cigarette advertisements were analyzed. Health claims appeared in 148 advertisments promoting a particular cigarette. One advertisement from the Tobacco Institute denied any link between secondhand (passive) smoke and cancer. There were 28 advertisements with health images. For all advertisements, 28.2 percent contained a health claim and 5.3 percent contained a health image. From 1964 to 1983, there were 108 health claims and 26 health images. There were more health claims and fewer health images than expected in advertisements appearing between 1964 and 1983.
Project Dates:
January 1984–April 1984.

0846. UNIVERSITY OF CHICAGO, ZOLLER DENTAL CLINIC, University of Chicago Hospital, 950 East 59th Street, Chicago, Illinois 60637.

Project Title:
Oral Aspects in Smoking.

Principal Investigator:
Fine, L.
Objective:
To develop a better understanding of the role of oral structures in smoking, e.g., the role of the lips and its effect on filter cigarettes.
Methods or Approach:
Lip pressure studies in normal smokers and of machine smoking will be conducted and lip coverage of filter will be measured.
Results to Date:
Preliminary results indicate that lip pressure and lip coverage parameters are important considerations in designing smoking machines that attempt to simulate human smoking.
Future Plans:
Parameters will be developed for studying lip action in relation to the filter in normal smoking and with artificial smoking.

0847. UNIVERSITY OF CHICAGO, 950 East 59th Street, Chicago, Illinois 60637.

Project Title:
Cocaine Effects in Man–Physiological and Behavioral.

Principal Investigator:
Fischman, M.W.
Objective:
To study the behavioral pharmacology of cocaine in humans and its interactions with alcohol, tobacco, marijuana, and diazepam.
Methods or Approach:
Research will characterize the behaviorally toxic and performance enhancing effects of cocaine and correlate these with its physiological and neurochemical effects. Pharmacokinetics will be studied using three routes of administration. Drug interactions will be investigated using a battery of behavioral and physiological measures already demonstrated to be sensitive to cocaine. Experimental analysis of variables relevant to drug self-administration will also be investigated, employing a

choice procedure using both intravenous and intranasal routes of administration, to determine the effects of various pharmacological and behavioral variables, including infusion duration, response cost, addition of a nondrug choice, pretreatment with dopaminergic blocking agents, and a comparison of the reinforcing efficacy of cocaine and methylamphetamine. Particular areas of interest are correlating measures of mood change and other subjective effects with drug choice to examine covariance. A profile of the cocaine user will be compiled (looking at variables such as drug-taking history and current drug use and relating these to relevant psychosocial variables).

Results to Date:
Results are not yet available.

Financial Support:
NIDA (5R01DA01491-08).

0848. UNIVERSITY OF CHICAGO, Department of Medicine, 5841 South Maryland Avenue, Chicago, Illinois 60637.

Project Title:
Induction of Hepatic Caffeine Demethase in Smokers.

Principal Investigators:
Schoeller, D.A.; Kotake, A.N.; Baker, A.L.

Objective:
To develop a noninvasive breath test based on caffeine demethylation to compare P$_1$-450 activity in smokers and nonsmokers.

Methods or Approach:
Interindividual differences in cytochrome P$_1$-450 activity and inducibility may influence an individual's susceptibility to cancers induced by exposure to polycyclic hydrocarbons: cigarette smoking is one of the major low level sources of such exposure. The breath test was validated in a rat model with i.p. administration of caffeine labeled with ^{14}C. Rats were placed in a sealed chamber and expired air was collected by passage through ethanolamine. Total ^{14}C expired in 20 min was collected and expressed as percent of dose. Similarity to P$_1$-450 activity was demonstrated by an eightfold induction of the breath test by 3-methylcholanthrene and no induction by phenobarbital. In vitro inhibition of caffeine demethylase by α-naphthoflavone and SKF-525F were characteristic of P$_1$-450. For human studies, caffeine labeled in the 3 position with the stable isotope ^{13}C was administered orally. Breath was collected before and 1 hour after dose; increase in $^{13}CO_2$ excretion was measured by isotope ratio mass spectrometry.

Results to Date:
In humans, 3-methyl-^{13}C-caffeine (3 mg/kg) tests were performed in 18 smokers and 44 nonsmokers. Results were expressed as percent dose/hour excretion of ^{13}C in breath CO_2 at 60 minutes after dose. Smokers (mean±SD) were induced by 50 percent relative to nonsmokers. Induction was not uniform in all smokers, nor were results distributed in a gaussian manner. There appeared to be two populations of nonsmokers, which were distributed in a 4 to 1 ratio with caffeine breath test mean values of 1.8 and 4.2 percent dose/hour. Distribution in smokers appeared to be trimodal, with a 5 to 7 to 6 distribution; however, more smokers must be studied before results are statistically significant. If trimodal distribution is assumed, mean caffeine breath test values for the three groups are 1.8, 4.0, and 5.2 percent dose/hour.

Future Plans:
The number of smokers will be increased to 50.

Project Dates:
1980–continuing.

0849. UNIVERSITY OF CHICAGO, Department of Medicine, 5841 South Maryland Avenue, Box 72, Chicago, Illinois 60637.

Project Title:
RCT of a Smoking Cessation Program on the Rate and Duration of Nonsmoking in Medical Patients With Smoking Related Illnesses.

Principal Investigator:
Silverstein, M.D.

Objective:
To determine if a smoking cessation program can increase and sustain smoking cessation rate in ambulatory patients with smoking-related illnesses, medical patients discharged from a hospital for smoking-related illnesses, and patients discharged from a hospital following admission to an intensive care unit for smoking-related illnesses.

Methods or Approach:
A randomized controlled trial of a smoking cessation program consisting of behavioral intervention, nicotine chewing gum, and group support will be applied to the three populations. Intervention will be designed to initiate and sustain nonsmoking behavior. Smoking cessation will be measured by self-report and objective measurements.

Results to Date:
Project is in a preliminary phase.

Future Plans:
If intervention is successful, it will be extended in each population to smokers at risk of experiencing a smoking-related illness.

Project Dates:
July 1985–July 1988.

0850. UNIVERSITY OF ILLINOIS AT CHICAGO, Department of Psychology, Box 4348, Chicago, Illinois 60680.

Project Title:
Attitude and Behavior Change in Smoking Cessation.

Principal Investigator:
Gruder, C.L.

Objective:
To identify attitude change procedures that will enhance maintenance of smoking cessation.

Methods or Approach:
A multifactor, behavioral smoking cessation treatment program is being modified to include a component designed to change participants' beliefs and attitudes in such a manner as to enhance maintenance of abstinence once it is achieved. This component comprises a procedure designed to induce cognitive dissonance; it is hypothesized that participants will eliminate the negatively affective state by adopting more antismoking attitudes, which will persist to support the change in smoking behavior. One group is exposed to the attitude change procedure in the context of treatment; a second group is "yoked" to the first and exposed to attitude change information, but not in a manner that should lead to persistence. A third group receives only behavioral treatment. Attitudes and smoking behavior are measured over 6 months.

Results to Date:
Preliminary analyses indicate that the expected pattern of attitude change that persists in the experimental condition, compared with control conditions, is not occurring. Attitudes toward target issues are changing in the antismoking direction in all conditions. Smoking rates decreased more in the experimental condition than in control conditions from pro-

gram onset to 1 month following end of the clinic. However, this was because smokers in the experimental condition were heavier smokers at program onset. There was no difference in attitude change between participants who achieved abstinence and those who did not. Followup telephone interviews are being conducted to determine attitudes and smoking status 6 months following end of treatment.

Project Dates:
July 1981–June 1985.

Financial Support:
NIDA (R01DA02581).

0851. UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN, Department of Health and Safety Studies, 1206 South Fourth Street, Room 117, Champaign, Illinois 61820.

Project Title:
Self-Efficacy as a Predictor of Smoking Behavior in Young Adolescents.

Principal Investigators:
Lawrance, L.; Rubinson, L.

Objective:
To apply Bandura's self-efficacy theory to prevention of adversive health behaviors such as cigarette smoking; (2) develop suitable self-efficacy scale for prediction of onset of smoking behavior in young adolescents; (3) diagnose specific areas of vulnerability to be targeted by intervention program; (4) discover stability of smoking behavior and circumstances under which it may occur; and (5) discern differences between males and females in perceptions of self-efficacy to resist smoking.

Methods or Approach:
A scale of 50 self-efficacy items was developed. The items, with self-reported smoking behavior and basic demographics, comprised the instruments. A sample of 800 sixth and seventh grade students were administered the survey on three occasions over an 8-month period (May 1984, September 1984, January 1985). Responses to self-efficacy items were subjected to factor analysis to determine relevant subscales. Scales were used in discriminant analysis to ascertain their capacity to predict smoking behavior.

Results to Date:
Results revealed three reasonably consistent factors concerning opportunities to smoke, emotional disturbances, and influence of friends. There was a relationship between total self-efficacy score and self-reported smoking behavior, suggesting that the instrument was a valid indicator of smoking behavior. Discriminant analysis provided significant functions for predicting smoking behavior on relatively close temporal phases of the project. Influence of friends persists as a major determinant of concurrent and future smoking activity. Indications were that self-efficacy could be refined and utilized effectively as a predictive and diagnostic tool in smoking education programs.

Future Plans:
The self-efficacy scale could be refined, reduced, and administered in conjunction with chemical analyses to ensure validity of self-report data. Administration of the scale to a different sample would ensure that the concept involved is accurately assessed. A modification of the scale to other abused substances would be beneficial.

Project Dates:
April 1984–May 1985.

0852. UNIVERSITY OF ILLINOIS, Department of Psychology, 605 East Daniels Street, Urbana, Illinois 61820.

Project Title:
Spectral Analysis as an Assessment Technique for Smoker Subtypes.

Principal Investigators:
Emmons, K.M.; Bernstein, D.A.

Objective:
To investigate the utility of spectral analysis as a behaviorally based assessment measure of smoking.

Methods or Approach:
It was hypothesized that an assessment device based on actual behavior in the natural environment would provide a better description of behavior than is possible with self-report techniques. In addition, it was postulated that spectral analysis would provide advantages over raw data plots across time because of its ability to remove noise components and to reveal structures not readily visible in raw data. The study involved 20 regular smokers who kept self-monitoring records for a 2-week period. Spectral analysis was done on the record, and the resulting spectral plots were analyzed for characteristics that allowed tenative subtyping of smoking based on either an addictive component or an environmental component. Correlational analyses were used to determine the relationship between the subtype decision, individual scores on the Horn-Waingrow Why Do You Smoke scale, and demographic variables. T-tests were used to determine if there were differences between proposed subtypes.

Results to Date:
Spectral plot structures allowed separation of smokers into two broad groupings: addicted smoking and environmental smoking. All subjects in the addictive category had similar periodicities, spectral peak structure, amplitude, and phase components, while the environmental group was very heterogeneous. Smokers with a major addictive component had significantly higher scores on the Horn-Waingrow scale. No differences were found between weekend and weekday smoking rate in the addicted subgroup, suggesting the presence of a stable process. The environmentally influenced subgroup had significantly higher scores on the positive affect subscale and smoked significantly more cigarettes on weekends than during the working week. The finding of more stable processes in the addicted subgroup provides some evidence for the subtype decision made based on spectral analyses. Spectral analysis offers advantages over raw data plots, cumulative records, and traditional analyses in that it removes variability and the associated error component from data and can reveal processes that are not readily visible. It has potential as an idiographic assessment technique that may improve treatment selection and outcome.

Future Plans:
A second project, currently in progress, will compare outcomes of individuals in different treatment programs, based on subtype classification.

Project Dates:
June 1982–completed.

Financial Support:
University of Illinois.

0853. UNIVERSITY OF ILLINOIS, COLLEGE OF MEDICINE, Department of Medicine, 840 South Wood Street, Chicago, Illinois 60612.

Project Title:
Sites of Action and Role of Mediators in Asthma.

Principal Investigator:
Lourenco, R.V.
Objective:
To (1) investigate the site of action in the lung of histamine and leukotrienes; (2) study the relationship of these substances to asthma; and (3) investigate the effect of cigarette smoking in the action of asthma mediators.
Methods or Approach:
Effects of histamine and leukotriene will be studied in asthmatic and healthy nonsmoking volunteers. In part 1, each subject will undergo four inhalation studies separated by at least a week. Each study will involve inhalation of radioaerosolized Fe_2O_3 followed by inhalation of a predetermined challenge dose of either histamine, leukotriene (LTD_4), isotonic saline, or nothing (control). Mucociliary clearance and tracheal mucociliary transport will be measured for 4.7 hours with a gamma camera and multidetector scintillation probe. In part 2, the effects of preferentially deposited histamine or LTD_4 on the lung will be examined. Using a breathing pattern for either central or peripheral deposition, subjects will inhale an Fe_2O_3 radioaerosol followed by mediator challenges with histamine or LTD_4. Partial flow volume loops will be recorded to determine response in central and peripheral airways.
Results to Date:
Project is in a preliminary phase.
Project Dates:
February 1985–February 1988.
Financial Support:
NHLBI (1R01HL/AI33461-01).

0854. UNIVERSITY OF ILLINOIS, COLLEGE OF MEDICINE, Department of Medicine, 840 South Wood Street, Chicago, Illinois 60612.

Project Title:
Research in Chronic Obstructive Lung Disease.

Principal Investigator:
Lourenco, R.V.
Objective:
To investigate the influence of developmental age on pulmonary deposition and clearance of inhaled particles; separate effects of cigarette smoking from effects of aging.
Methods or Approach:
The baboon was chosen as an animal model to help understand the characteristics of mucociliary transport in the maturing human lung. Lung mucociliary clearance in the baboon is measured using radioaerosol techniques from birth through the first 5 years of life. Newborn baboons are hand raised. At predetermined intervals, they inhale a radiolabeled aerosol. Immediately, lung mucociliary clearance is measured for 3 hours by positioning the unanesthetized baboon in a special restraining chair in front of a gamma camera.
Results to Date:
Mucociliary transport studies up to 1 year of age indicate that neither aerosol deposition nor lung mucociliary clearance change significantly with age. Findings suggest that mucociliary transport rates within airways increase with developmental age to compensate for longer airway length.
Project Dates:
July 1981–January 1985.
Financial Support:
VA.

0855. UNIVERSITY OF ILLINOIS, 2300 Formfit Building, Chicago, Illinois 60680.

Project Title:
Smoking Intervention Evaluation.

Principal Investigators:
Warnecke, R.B.; Corrigna, K.
Objective:
To examine the impact of a televised smoking cessation program offered in the Chicago metropolitan area in January 1985.
Methods or Approach:
Three waves of telephone interviews (in January–February and April–May 1985 and January–February 1986) will be conducted. Approximately 1,000 persons who reside in the WMAQ-TV broadcast area and who filled out registration forms for the "Fredom from smoking in 20 Days" program will be contacted.
Results to Date:
Project is in a preliminary phase.
Financial Support:
NCI; Illinois Cancer Council.

0856. VETERANS ADMINISTRATION MEDICAL CENTER, 333 East Huron Street, Chicago, Illinois 60611.

Project Title:
Endoscopic Survey of Esophageal Dysplasia Using Lugol's Solution and Esophageal Brush Cytology and Biopsy.

Principal Investigators:
Layden, T.J.; Schlesinger, P.
Objective:
To study 100 patients who are at high risk for developing cancer of the esophagus; determine whether Lugol staining of the esophagus during endoscopy will detect dysplastic lesions.
Methods or Approach:
Patients who undergo endoscopy for other purposes will be included in the study if they are more than 40 years of age and have a significant history of alcohol and tobacco use. The esophagus will be examined with endoscopy and sprayed with Lugol's stain; unstained areas will be brushed and biopsied. Specimens will be then examined for dysplasia.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1983–continuing.
Financial Support:
VA.

0857. VETERANS ADMINISTRATION, Roosevelt Road at Fifth Avenue, Hines, Illinois 60141.

Project Title:
Role of Diet in the Production of Bacterial Enzymes Implicated in Carcinogenesis of the Human Gastrointestinal Tract.

Principal Investigators:
Sontag, S.J.; Gelbart, S.
Objective:
To determine whether mutagenic compounds are excreted in the urine of smokers, patients with cirrhosis, and normal controls.
Methods or Approach:
First morning urines were discarded, and all urine for the next 12 hours was collected, frozen, and analyzed the next day. Urine from 5 cirrhotics, 12 smokers, and 15 healthy controls

was analyzed using the assay methods of Yamasaki and Ames with and without sulfatase and glucuronidase, and the bacterial strains were incubated for 72 hours. All subjects ate a standard diet.

Results to Date:
Eleven of the smokers had mutagenic urine. Of the 17 samples collected, 16 were mutagenic. Thirteen of the nonsmoking controls had nonmutagenic urine; of the 24 samples collected, 22 were nonmutagenic. All 12 samples collected from the 5 cirrhotics were mutagenic. It is concluded that nonsmoking patients with cirrhosis excrete mutagens in the urine.

Financial Support:
VA.

0858. VETERANS ADMINISTRATION, Roosevelt Road at Fifth Avenue, Hines, Illinois 60141.

Project Title:
Epidemiologic Investigation of Tobacco Usage and Disease Development.

Principal Investigator:
Sharp, J.

Objective:
To assess the role of tobacco and other environmental factors in the etiology of myocardial infarction (MI) and cancers of the lung, oral cavity, esophagus, bladder, and pancreas.

Methods or Approach:
An epidemiologic, retrospective, case–control methodology was used. Index cases were drawn from patients admitted with a diagnosis of either cancer of the lung, bladder, pancreas, upper alimentary or respiratory tract, or MI. Cancer cases were restricted to patients aged 20 to 80 with diagnosis in the first 6 months. MI cases were restricted to those admitted for the first occurrence of the event and are 20 to 65 years of age. Two sets of controls were used: a matched hospital control for each case consisting of patients with cancer of sites other than index disease and index disease-free residental neighbors. A pretested, standardized, forced-choice data collection instrument was administered to all subjects, including controls, by trained interviewers. The questionnaire was designed to measure demographic, smoking, and a wide variety of other environmental and clinical variables.

Results to Date:
Data collection and analysis are completed.

Financial Support:
VA.

Indiana

0859. INDIANA UNIVERSITY, Department of Health and Safety Education, HPER Building, Room 116, Bloomington, Indiana 47405.

Project Title:
Operation Smart Decision: An Intervention Project to Deter Cigarette Smoking and Alcohol Abuse in Monroe County, Indiana, Children and Adolescents.

Principal Investigators:
Seffrin, J.R.; Bailey, W.J.

Objective:
To design, implement, and evaluate a multivariate instructional message, on a multilevel community basis, to deter cigarette smoking and the abuse of alcohol in the "under 25" population in Monroe County, Indiana.

Methods or Approach:
This project began as part of the National Health Education–Risk Reduction program. Emphasis is placed on decisionmaking skills, resistance to peer influence, self-concept, substitution of role models, and changes in perceptions about smoking and alcohol abuse in the instructional message used in this project. The program will operate at three levels; adolescents (middle school and high school), college students (who act as role models), and community (to reinforce the message for the adolescents). A longitudinal prevalence study will examine changes in prevalence over time. Additional data on "social indicators" is being collected in the alcohol portion of the study, and a time-series prospective model is being used. A major "qualitative/naturalistic" evaluation will be used to identify benefits and/or problems which cannot be identified using traditional quantitative methods.

Results to Date:
Preliminary data indicate knowledge change occurs. However, the major portion of this study is still in progress, and data collection will not be complete for another 5 years.

Future Plans:
Strategies for future years of the intervention project will be derived from the findings of the completed years.

Project Dates:
October 1980–1987.

Financial Support:
Indiana University; PHS (H11/CCH500249-03-2); Indiana State Board of Health.

0860. INDIANA UNIVERSITY, CENTER FOR HEALTH AND SAFETY STUDIES, HPER Building, Bloomington, Indiana 47405.

Project Title:
Message Source Credibility in Drug Education.

Principal Investigator:
Bailey, W.J.

Objective:
To identify potential attributed message sources that are perceived by students to be the most credible sources of information in various drug education strategies and settings.

Methods or Approach:
Drugs to be studied include tobacco, alcohol, narcotics, and fictitious drugs. Expertise, trustworthiness, and appearance of the communicator will be included as subcategories of message source credibility. Self-reports from subjects will be used to identify potential message sources that appear to be most credible to various categories of students. An experimental protocol will expose subjects to an identical message attributed to different message sources. Subjects' acceptance or rejection of the message will be measured using a written instrument now being developed. Message acceptance or rejection will be compared with attributed communicator status as a credible message source.

Results to Date:
Results are not yet available.

Project Dates:
September 1982–December 1986.
Financial Support:
Indiana University Center for Health and Safety Studies.

0861. INDIANA UNIVERSITY, SCHOOL OF DENTISTRY AND SCHOOL OF MEDICINE, 415 North Lansing Street, Indianapolis, Indiana 46202.

Project Title:
Physician/Dentist Interventions for Smoking Cessation.

Principal Investigators:
Cohen, S.J.; Stookey, G.K.
Objective:
To identify the most effective intervention method for physicians and dentists to use to help patients quit smoking and maintain cessation; evaluate the adaptation and effectiveness of the best smoking intervention condition with a new cohort of physicians and dentists.
Methods or Approach:
Intervention methods to be evaluated are (1) advice, in which the doctor advises patients to quit smoking using a step-care system (i.e., identify smoking status of patient, deliver a firm quit smoking message, get patient to agree to a quit date, and follow up patient progress); (2) nicotine chewing gum, in which the doctor uses the advice method and prescribes nicotine chewing gum to help patients in cessation efforts; (3) reminder/feedback, which utilize the advice method plus placement of stickers on patient records to alert doctor to discuss smoking with patient and a summary feedback report given to the doctor on a bimonthly basis that identifies patient/doctor interactions; and (4) Nicorette and reminder/feedback, which uses of all of these methods.
Results to Date:
Project is in a preliminary phase.
Project Dates:
August 1984–July 1989.
Financial Support:
NCI (1R01CA38337-01).

0862. PURDUE UNIVERSITY, Department of Medicinal Chemistry and Pharmacognosy, West Lafayette, Indiana 47907.

Project Title:
Modifiers of Chemical Carcinogenesis in Cell Culture.

Principal Investigator:
Baird, W.M.
Objective:
To determine how modifiers of carcinogenesis such as cocarcinogens and tumor promoters affect the metabolic activation of and induction of biological effects by carcinogenic polycyclic aromatic hydrocarbons.
Methods or Approach:
Humans are constantly exposed to the vast mixture of chemicals that are present in the environment. Often this mixture (e.g., urban air) contains both carcinogenic polycyclic aromatic hydrocarbons and other types of polycyclic hydrocarbons that can act both as cocarcinogens with some carcinogenic hydrocarbons and as inhibitors of carcinogenesis with others. In addition, mixtures such as cigarette smoke contain other classes of chemicals which can alter the effects of exposure to carcinogenic polycyclic hydrocarbons by acting as cocarcinogens or as tumor promoters. Their effects on the metabolic activation of carcinogenic polycyclic aromatic hydrocarbons and the induction of biological effects will be measured in hamster embryo cell cultures. These studies will include quantitative measurements of hydrocarbon oxidation, conjugation, DNA-interaction products, and the induction of cytotoxicity, cell-mediated mutation, and transformation. The role of conjugation of hydrocarbon metabolites to glucuronic acid in the induction of biological effects will be examined. The effects of other types of modifers such as cocarcinogens of other classes and tumor promoters on the above parameters will also be measured. The results obtained will be of use in predicting how the effects of exposure to carcinogens are altered in the presence of hydrocarbons and other types of cocarcinogens and tumor promoters. This will permit modification of these effects and aid in the development of short term assays with enhanced sensitivity for the detection of carcinogens in the environment.
Results to Date:
It has been demonstrated that in hamster embryo cell cultures the cocarcinogen benzo(*e*)pyrene (BeP) inhibits the metabolism of the carcinogen benzo(*a*)pyrene (BaP) but increases the proportion of BaP converted to a proximate carcinogenic metabolite, the 7,8-dihydrodiol. The BaP-DNA interaction products formed in cells treated with various concentrations of BeP have been characterized, and it was found that there is a dose-dependent decrease in the amount of BaP bound to DNA in cells exposed to BeP. As the concentration of BeP increased (0, 1.0, 2.0, and 5.0 μg/ml), the amount of BaP bound to DNA decreased (38.9, 18.6, 15.5, and 11.2 pmoles BaP/mg DNA, respectively).
Future Plans:
Future objectives are to (1) determine the effects of the cocarcinogens benzo(*e*)pyrene, pyrene, and benz(*a*)anthracene on the binding of BaP and 7,12-dimethylbenz(*a*)anthracene (DMBA) to DNA in hamster embryo cells; and (2) determine the effect of cocarcinogen treatment time and dose on induction of mutations by BaP and DMBA in the hamster embryo cell mediated V79 cell mutation assay. Studies will aid in determining how weakly carcinogenic hydrocarbons that are either good or poor inducers of hydrocarbon metabolizing enzymes alter the metabolic activation and detoxification of unsubstituted BaP and methyl-substituted (DMBA) carcinogenic hydrocarbons in cells, and will help to establish the role of particular hydrocarbon–DNA adducts in the induction of biological effects.
Project Dates:
July 1976–1986.
Financial Support:
NCI (CA 28825).

0863. ST. ELIZABETH HOSPITAL MEDICAL CENTER, Box 7501, Lafayette, Indiana 41904.

Project Title:
Four-Step Stop Smoking Intervention Program.

Principal Investigators:
Jones, J.R.; Dewey, J.E.
Objective:
To (1) identify a personality profile of individuals who attend a smoking cessation program; (2) determine success rate of a four-session behavior modification stop smoking program; and (3) develop predictive categories of questions for individuals who need more assistance in the quitting process.
Methods or Approach:
Each participant was administered an 18-item pretest at entry to the program. The test was self-scored and returned. A four-session, behavior modification, group support approach was used that allowed participants to develop their own quit plan.

Instruction covered the withdrawal syndrome, stress management, weight control, and crisis planning. Participants were given a series of structured activities for the 12 days following the last week of the program. After 6 months, a followup questionnaire was sent to participants. If no response was received in 2 weeks, a phone call was made to collect followup information.

Results to Date:

Between December 1982 and May 1983, 108 persons (54 males and 54 females, average age 41.7 years) participated in the program. Pretest data showed mean number of years smoked was 22.6, mean number of cigarettes smoked/day was 33.1, mean age of regular smoking was 19.1 years. Approximately 80 percent had previously tried to quit; average number of attempts was 2.0. At the end of the program, 68 percent were abstinent; at 6-month followup, 50 percent were still not smoking. Heavy smokers (> 1.5 packs/day) had an easier time quitting. Among successful quitters, the most common reason given for wanting to stop was "just for myself." Success rate was higher among participants who attended all sessions and no person who left the program still smoking had quit at followup.

Future Plans:

Followup will continue every 6 months to evaluate long-term success.

Project Dates:

December 1982–continuing.

Iowa

0864. DUBUQUE EMPHYSEMA AND BRONCHITIS FOUNDATION, 2095 Kennedy Road, Dubuque, Iowa 52001.

Project Title:

Cigarette Design for Minimizing Escaping of Cigarette Smoke.

Principal Investigator:

Chun, N.

Objective:

To minimize smoke from lighted cigarettes.

Methods or Approach:

Cigarettes are being designed with smoke-absorbing material to minimize smoke emission.

Results to Date:

Results are not yet available.

0865. IOWA LUTHERAN HOSPITAL, University at Penn Avenue, Des Moines, Iowa 50316.

Project Title:

Alpha Radioactivity in Cigarette Smoke Filtrates.

Principal Investigator:

Vandeberg, J.

Objective:

To determine levels of alpha radioactivity in cigarette smoke; determine source(s) and potental damage to lung parenchyma.

Methods or Approach:

Several brands of cigarettes will be smoked by machine and aerosols deposited on appropriately sized filter. Alpha levels of radioactivity will be measured and compared with control and background levels. Sources of greater than normal levels will be identified.

Results to Date:

Significantly high levels of alpha radioactivity existed in filtrates of all substances burned. Levels are potentially dangerous. Further research will be conducted.

Project Dates:

May 1983–continuing.

Financial Support:

Iowa Lutheran Hospital.

0866. IOWA STATE UNIVERSITY, Department of Psychology, Ames, Iowa 50011.

Project Title:

Spectral Analysis as an Assessment Device for Smoker Subtypes: A Validation Study.

Principal Investigators:

Emmons, K.M.; Lando, H.A.

Objective:

To determine the construct validity of spectral analysis as a behaviorally based assessment device.

Methods or Approach:

It is hypothesized that smokers with a major addictive component will be more successful in treatment programs with a nicotine gum component than in behavioral treatment alone. It is also predicted that the outcome for environmental smokers will not be improved by the addition of nicotine gum to the behavioral treatment package. Sixty smokers were randomly assigned to three treatment conditions: (1) broad-spectrum behavioral treatment, (2) behavioral treatment plus nicotine gum, and (3) nicotine gum only. One week pretreatment self-monitoring data were collected and spectral analysis was done. Outcome data will be collected for 1 year following treatment.

Results to Date:

Treatment is currently in progress for the behavioral treatment group; 3-month followup has been completed for the nicotine gum only group.

Project Dates:

June 1984–January 1986.

Financial Support:

University of Iowa.

0867. IOWA STATE UNIVERSITY, Department of Psychology, Ames, Iowa 50011.

Project Title:

Long-Term Modification of Chronic Smoking Behavior.

Principal Investigator:

Lando, H.A.

Objective:

To (1) determine a clinically effective treatment intervention that is both safe and widely applicable and that can be implemented by trained lay facilitators; (2) test a specific cohesiveness manipulation and assess its impact on both process and outcome measures; (3) assess the relative contribution of cohesiveness intervention to aversive (satiation) and nonaversive (nicotine fading) treatments; (4) quantify cohesiveness construct so that it can be more readily defined and applied not only in smoking cessation programs but also in other group treatment contexts; and (5) assess additional subject and process variables (e.g., self-efficacy, smoking history, environmental stressors) and determine relationship with long-term outcome.

Methods or Approach:

A clinically effective procedure (40 percent 1-year abstinence) has been derived, which entails an unpleasant and potentially risky satiation technique that has limited subject acceptability. Recent work has focused on a more acceptable nicotine-fading procedure, unfortunately it has produced less consistent outcomes. Group process, especially group cohesiveness, had been largely overlooked in previous investigations. Aversion may promote cohesiveness through a shared unpleasant experience; however, other methods for promoting cohesion may be available. A 2 x 2 experimental design is being used with 480 subjects assigned to aversive or nonaversive treatment and to special cohesiveness training or a standard comparison condition.

Results to Date:

Final results are not yet available, but preliminary data indicate that cohesiveness may be facilitated by specific group exercises, modeling of appropriate behavior, and contractual agreements outlining desired interaction.

Future Plans:

Long-term followup of study participants will focus on predictive value of numerous process variables, including self-efficacy and perceived environmental support, with close attention to the subsequent smoking history of initially nonabstinent subjects.

Project Dates:

January 1984–December 1985.

Financial Support:

ACS (PBR-7).

0868. IOWA STATE UNIVERSITY, Department of Veterinary Anatomy, Ames, Iowa 50111.

Project Title:

Morphological Evaluation of the Lungs From Twenty Stump-Tailed Macaques.

Principal Investigator:

Adams, D.R.

Objective:

To examine lungs from monkeys that received a high-fat diet and an aerosol of tobacco smoke; study epithelia from airways and alveoli to determine relative densities of cell types present, histochemical characteristics, and volume fractions of subcellular contents.

Methods or Approach:

Compound light, transmission electron, and scanning electron microscope (SEM) examinations will be performed. Alcian Blue (pH 1.0 and 2.5)/periodic acid-Schiff's reagent will be used to determine presence of neutral and siliated or sulphated acid glycoproteins. The Leitz Bioquant II Image Analysis System will supply data on volume fractions of nucleus, secretary granules, mitochondria, endoplasmic reticulum, and free ribosomes.

Results to Date:

Five lung tissues from each monkey, embedded in epon/araldite, were sectioned at 1.0 μm. Tissues were excised from two regions of the right cranial lobe, one region of the right middle lobe, and two regions of the right caudal lobe. Seven light micrographs of alveoli from the dorsal portion of the right cranial lobe were studied to determine volume density of alveolar air space. The four remaining lung tissues will also be photographed and quantified. A tissue from the right cranial lobe of each monkey was examined with the scanning electron microscope. Eight micrographs of each tissue, taken at 400X magnification, will be used to determine the relative number of alveolar pores. Epithelia of subsegmental bronchi from the right cranial lobe were also examined with SEM. The barrier thickness of the interalveolar septa is being determined, using electron micrographs of the gas exchange area from the right cranial lobe.

Project Dates:

February 1983–February 1985.

Financial Support:

USDA (IOWV-400-23-90).

0869. UNIVERSITY OF IOWA, Department of Pediatrics, Iowa City, Iowa 52242.

Project Title:

Pharmacologic Management of Children With Asthma.

Principal Investigator:

Weinberger, M.M.

Objective:

To assess the outcome of children with chronic symptoms of asthma, managed with prophylactic long-term medication; identify the variables (age, sex, severity of asthma, presence of history of atopic dermatitis, and cigarette smoking) that relate to the medication requirement for control of symptoms.

Methods or Approach:

Subsequent requirements for continued prophylactic medication will be studied in a double-blind (theophylline–placebo) controlled trial every 12±1 months during periods when patients' asthma symptoms are expected to be severe. The effect of short course corticosteroid therapy on bronchodilator responsiveness of asthmatic children whose airways obstruction is initially not responsive to noncorticosteroid medication will be studied in double-blind fashion. Subsequent followup of patients will show if airway obstruction in children who receive short-term corticosteroid therapy is more responsive for longer periods to noncorticosteroid bronchodilators than those who do not receive corticosteroids.

Results to Date:

Project is in a preliminary phase.

Financial Support:

NIAID (5R01AI16151-05).

0870. UNIVERSITY OF IOWA, Department of Pediatrics, Iowa City, Iowa 52242.

Project Title:

Relationship of Parental Smoking and Gas Cooking to Respiratory Disease in Children.

Principal Investigators:

Ekwo, E.E.; Weinberger, M.M.; Lachenbruch, P.A., et al.

Objective:

To examine the relationship of parental smoking and gas cooking on the occurrence of respiratory illness and symptoms in children and to study the relationship between these environmental exposures and pulmonary function.

Methods or Approach:

Questionnaires were sent home with children in participating schools (87 percent of 6- to 12-year-old children in an Iowa City school district, which serves a university community). Pulmonary function measurements were obtained from 47 girls and 41 boys whose parents did not smoke and 52 girls and 42 boys whose parents were smokers. Children were excluded if there was a history of recurrent respiratory illness or if there was any history of upper or lower respiratory infection during the prior 6 months. Discrete multivariate analysis was used to study interactions among factors.

Results to Date:

Completed questionnaires were obtained for 1,355 children (65.7 percent of those aged 6 to 12 years in the school district). The risk of hospitalization for respiratory illness before the age of 2 years was increased when gas was used for cooking ($p < 0.001$) or at least one of the parents smoked ($p < 0.02$). The occurrence of cough with colds in children was significantly increased when one or both parents smoked ($p < 0.001$). Small but significant increases ($p < 0.05$) in mean values of forced expiratory volume in 1 sec, flow rate at 75 percent of forced vital capacity, and forced expiratory flow rate from 25 to 75 percent of vital capacity were seen after administering inhaled isoproterenol to children whose parents smoked (94) but not among children whose parents did not smoke (89). This was not seen in association with gas cooking. Exposure of children during the first 2 years of life to gas cooking or cigarette smoking appears to be associated with an increased risk of hospitalization for respiratory illness, and cigarette smoking appears to be associated with a more consistent response to inhaled bronchodilator among 6- to 12-year-old children with no other history of chronic respiratory illness.

Financial Support:

Clinical Research Center (RR59); NIH (1RO1AI16151-01); Cystic Fibrosis Foundation (C 521A); Johnson County Lung Association.

Reference:

Ekwo, E.E.; Weinberger, M.M.; Lachenbruch, P.A., et al. "Relationship of Parental Smoking and Gas Cooking to Respiratory Disease in Children." *Chest* 84(6):662-668, December 1983.

0871. UNIVERSITY OF IOWA, TOXICOLOGY CENTER, Department of Pharmacology, Iowa City, Iowa 52242.

Project Title:

Pancreatic Carcinogen-Metabolizing Enzymes.

Principal Investigator:

Baron, J.

Objective:

To investigate and determine the biochemical basis for pathogenesis of chemically induced exocrine pancreatic cancer; identify the cell of origin of 7,12-dimethylbenz(*a*)anthracene-induced adenocarcinomas in the rat exocrine pancreas.

Methods or Approach:

7,12-Dimethylbenz(*a*)anthracene-containing beeswax implants were sutured onto rat pancreases, and rats were killed after various periods of exposure to polycyclic aromatic hydrocarbon. Exocrine pancreatic cells were phenotyped for the following carcinogen-metabolizing enzymes: cytochrome P-450 BNF-B and PB-B (the major forms of microsomal cytochrome P-450 induced in rat liver by β-naphthoflavone and phenobarbital, respectively); NADPH-cytochrome P-450 reductase; epoxide hydrolase; and glutathione S-transferases B, C, and E. Cells of origin of 7,12-dimethylbenz(*a*)anthracene-induced exocrine pancreatic lesions were identified by phenotypic staining for the enzymes.

Results to Date:

Although 7,12-dimethylbenz(*a*)anthracene did not induce formation of adenocarcinomas in the rat pancreas, it did result in the appearance of eight different cell types within the exocrine pancreas. It was concluded that the cell types that exhibited preneoplastic characteristics had arisen from acinar cells, supporting previous findings.

Project Dates:

July 1981–June 1985.

Financial Support:

NCI (CA30140).

0872. UNIVERSITY OF IOWA, TOXICOLOGY CENTER, Department of Pharmacology, Iowa City, Iowa 52242.

Project Title:

Carcinogen-Metabolizing Enzymes of the Respiratory Tract.

Principal Investigator:

Baron, J.

Objective:

To determine where carcinogen-metabolizing enzymes are localized within the respiratory tract, where they can be induced within this organ system, and how their cellular localizations relate to induction of carcinogenesis.

Methods or Approach:

Quantitative and qualitative immunohistochemical staining techniques are being employed with enzyme histochemical methods to determine (1) where carcinogen-metabolizing enzymes are localized within the lung; (2) where enzymes are induced within the lung; and (3) alterations in enzymes and cells during development of benzo(*a*)pyrene (BaP)-induced pulmonary neoplasms. Enzymes being examined include cytochrome P-450 isozymes, glutathione S-transferase isozymes, NADPH-cytochrome P-450 reductase, and epoxide hydrolase. BaP hydroxylase activity is being investigated using a fluorescence histochemical procedure.

Results to Date:

Except for one isozyme of cytochrome P-450 (cytochrome P-450 MC-B), all enzymes were detected within bronchial and bronchiolar epithelia and in alveolar wall cells in lungs of untreated rats. Nonciliated bronchiolar epithelial cells (Clara cells) appear to contain the highest amounts of enzymes. Treatment of rats with 3-methylcholanthrene resulted in increased staining of Clara cells and alveolar wall cells for cytochromes P-450 BNF-B and MC-B. Treatment with Aroclor 1254 also resulted in increased staining for the two enzymes within Clara cells and alveolar wall cells, and also within bronchial epithelial cells.

Future Plans:

A BaP-ferric oxide mixture will be administered intratracheally to Syrian golden hamsters to induce formation of pulmonary neoplasms, and alterations in localizations of pulmonary carcinogen-metabolizing enzymes will be determined at various stages during carcinogenesis. An attempt will be made to identify the cell of origin of BaP-induced pulmonary lesions.

Project Dates:

April 1984–March 1989.

Financial Support:

NIGMS (GM33253).

0873. UNIVERSITY OF IOWA, UNIVERSITY HOSPITALS AND CLINICS, Division of Pediatric Cardiology, Iowa City, Iowa 52242.

Project Title:

Smoking in School Age Children: The Muscatine Study.

Principal Investigators:

Lauer, R.M.; Akers, R.; Krohn, M.D.

Objective:
To (1) conduct research into the correlates and explanation of adolescent smoking behavior; (2) develop an in-school smoking education/prevention program guided by research findings and findings of previous studies; and (3) evaluate short- and long-term effectiveness of the program in preventing or delaying onset of smoking among adolescents.

Methods or Approach:
The study population consisted of junior and senior high school students (grades 7 through 12, aged 12 to 18 years) in Muscatine, Iowa, who were followed over a 5-year period as they moved to each successive grade. Three measures were employed in the longitudinal study: (1) self-report questionnaire administered annually to all students; (2) biochemical measurement of smoking (saliva thiocyanate level); and (3) randomized question response, which is an anonymous form of self-report used to determine group-level smoking rates. A method developed and validated for measuring smoking behavior was used to determine risk factors for initiation, development, and maintenance of smoking. Tests of social learning theory and social bonding theory were also completed to explain adolescent smoking behavior. The project was an interdisciplinary effort involving medical, sociological, and education personnel and techniques.

Results to Date:
A social process model of deviant behavior, which incorporates constructs from social bonding and differential association theories, was developed to explain adolescent cigarette smoking. Data indicate that association with smoking peers has a substantial impact on subsequent smoking. A weakening of adolescents' beliefs in conventional values (e.g., nonsmoking behavior) increased the probability of having friends who espouse deviant values and/or behave in a deviant or nonconventional manner. The school was identified as the critical arena through which ties to the conventional belief system were maintained or weakened. Disaffection with school and related activities allowed the adolescent to be influenced by peers who engaged in some forms of misbehavior, such as cigarette smoking. Implications for smoking prevention programs indicate that exploring ways to tie disaffected students back into the school and its related activities might be a useful and/or necessary component of a prevention program. Although evaluation of the pilot education/prevention program indicated an attitudinal change toward nonsmoking behavior by students, no differences in smoking prevalence or behavior were found. The smoking prevention program has since been revised and is the primary focus for a new program involving seven middle schools in three eastern Iowa communities.

Project Dates:
July 1979–June 1984.

Financial Support:
NHLBI (HLR01HL20124; 1R18HL32847-01).

0874. UNIVERSITY OF IOWA, UNIVERSITY HOSPITALS AND CLINICS, Division of Pediatric Cardiology, Iowa City, Iowa 52242.

Project Title:
A School and Community Based Smoking Intervention Program.

Principal Investigators:
Lauer, R.M.; Krohn, M.; Becker, S., et.al.

Objective:
Design and implement a multidimensional antismoking program for teenagers directed at the psychosocial determinants of smoking; provide tools for resisting pressures to smoke.

Methods or Approach:
Cigarette smoking has multiple deleterious effects on health. Smoking experimentation occurs most often during early teenage years, and adolescents who acquire the habit tend to become lifelong smokers. Specific objectives are to (1) educate adolescents about the social and health consequences of smoking; (2) test and demonstrate the utility of competition and reward as means of reducing cigarette use in intra/interschool and intercommunity situations; (3) evaluate effectiveness of each component (school curriculum, competition, reward, community press) individually and in combination; and (4) continue basic research into determinants of adolescent smoking. The target population consists of public school students in the seventh grade in three similar Iowa communities who are initially surveyed in the fall for smoking prevalence (self-reported and salivary thiocyanate analysis), attitudes, and knowledge about smoking. The communities receive varying interventions, ranging from school curriculum alone to school curriculum plus community press. All interventions are associated with systems of competition and reward. Varying the intensity of treatment makes it possible to assess the contribution of each variable to adolescent smoking behavior. In the spring, students are resurveyed to assess behavioral or attitudinal changes. Students are followed in successive school years to determine any lasting effects of the interventions received. The project is a multidisciplinary effort.

Results to Date:
Project is in a preliminary phase.

Future Plans:
If evaluation shows the program to be effective, it will provide a tested comprehensive adolescent smoking prevention program that may be transferable to other school districts and communities.

Project Dates:
July 1985–June 1987.

Financial Support:
NHLBI (1R18HL32847-01).

0875. UNIVERSITY OF IOWA, COLLEGE OF DENTISTRY, N406 DSB, Iowa City, Iowa 52242.

Project Title:
Permeability of Skin and Oral Mucosa to Lipid Soluble Substances.

Principal Investigator:
Squier, C.A.

Objective:
To (1) measure and compare permeability of porcine skin and keratinized and nonkeratinized oral mucosa to lipid soluble substances; (2) visualize pathways taken by lipid soluble substances in traversing epithelia and any barriers encountered; (3) examine classes of lipids present in epidermis and oral epithelium; and (4) determine whether results can be correlated with measured permeability of tissues.

Methods or Approach:
Transepithelial flux is measured in perfusion chambers with radioisotopes. Pathways taken by substances traversing epithelia is determined by light and electron microscopic autoradiography of normal and freeze-dried tissue using radiolabeled molecules. Lipid content of epithelia is determined by thin-layer chromatography of solvent-extracted material.

Results to Date:
Skin, attached gingiva, and floor of mouth mucosa all show increased permeability to 0.01 percent nitrosonornicotine (NNN) when combined with 50 percent ethanol over that of NNN alone. Buccal mucosa shows a significant decrease in

permeability to NNN under these conditions. The principal pathway for all compounds across stratified squamous epithelium of skin and oral mucosa is via the intercellular route rather than through the cells. Keratinized oral epithelium (gingiva) has a very similar pattern of lipid composition to that of epidermis. In particular, the same types of ceramides are present that are believed to have an important role in forming the barrier to water permeation in skin. These similarities probably account for the similar water permeability properties of skin and keratinized oral mucosa. Nonkeratinized oral epithelia have a different lipid content from keratinized tissues, lacking ceramides, but containing large quantities of glycolipid (glycosylceramides) and probably glycoprotein.

Project Dates:
January 1983–December 1985.

Financial Support:
Smokeless Tobacco Research Council.

Kansas

0876. KANSAS DEPARTMENT OF HEALTH AND ENVIRONMENT, Division of Health, Forbes, Topeka, Kansas 66620.

Project Title:
The Kansas Smoke Avoidance Program: Project VOTE.

Principal Investigator:
Hollowell, J.G.

Objective:
To provide a low-cost public health program with the goal of reducing exposure of workers to secondhand smoke.

Methods or Approach:
In 1983, a task force on the hazards of tobacco consumption was established at the Kansas Department of Health and Environment. In 1984 it expanded and became an interdepartmental task force for the purpose of assisting Kansas public and private employers in establishing smoke avoidance programs and to make Kansans aware of the hazards of tobacco consumption and the benefits of quitting. The task force sponsors statewide health promotion efforts relevant to the hazards of tobacco use, such as the Great American Smokeout. Project VOTE, established in October 1982, is not a program to ban smoking at work, but seeks to accommodate both those who smoke and those who don't in a democratic manner. If a vote by employees is favorable, smoking is permitted only in designated areas. Smoking cessation programs are offered to workers who would like to quit. Alternatives to voting are also available, such as questionnaires and draft administrative directives. A portfolio of material is available that contains a sample ballot, a model smoking policy, hints on how to organize a VOTE program, a fact sheet on the harmful effects of secondhand smoke, and samples of health education and promotional materials. Technical assistance in developing a smoke avoidance program is available on request.

Results to Date:
Three of the largest State agencies have adopted a smoke avoidance policy and two others are considering adopting a policy. All but 10 of the local health departments voted to adopt the policy within the first month following initiation of the program. A number of health care facilities have adopted VOTE. Approximately 1,000 kits have been sent out.

Financial Support:
Kansas Department of Health and Environment.

0877. UNIVERSITY OF KANSAS MEDICAL CENTER, Building 48, Room 225, Rainbow Boulevard at 39th Street, Kansas City, Kansas 66103.

Project Title:
Follow-up Studies on Improperly Grown Human Fetuses.

Principal Investigators:
Holmes, G.E.; Miller, H.C.

Objective:
To study children who as infants had a combination of two intrauterine growth retardation (IUGR) patterns (low ponderal index and short-for-date); compare current growth and development with that of children with only one pattern or with neither.

Methods or Approach:
It is hypothesized that children with combined IUGR patterns are at greater risk for a high incidence of congenital anomalies and will have had significant problems with somatic growth and psychomotor development, and that mothers of these infants will have had a larger number of adverse maternal behavioral factors during pregnancy than mothers of other groups. Children in the study cohort are from an original infant group with birth data collected between 1973 and 1978. Original maternal and neonatal data, hospital charts, and clinical records will be studied. A letter and medical history questionnaire will be sent to parents, and a brief physical exam will be performed whenever possible. Attention will be given to current somatic measurements and to general health and developmental progress. Findings will be correlated with previously defined maternal behavioral factors associated with pregnancy (e.g., maternal age, weight gain, smoking status, prenatal care). Previous studies found significant differences in postnatal somatic growth patterns for infants with either type of IUGR and a high incidence of congenital problems in short-for-date infants. Fetal growth outcome was correlated with maternal factors, including cigarette smoking.

Results to Date:
Data collection is in progress; results are not yet available.

Project Dates:
April 1984–April 1986.

Financial Support:
University of Kansas Medical Center.

0878. UNIVERSITY OF KANSAS, COLLEGE OF HEALTH SCIENCES, Rainbow Boulevard at 39th Street, Kansas City, Kansas 66103.

Project Title:
Factors Associated With Morbidity Among Breast Fed and Formula Fed Babies.

Principal Investigators:
Holmes, G.E.; Hassanein, K.M.; Miller, H.C.

Objective:
To determine what effect various maternal and family factors as well as the infant feeding mode have on morbidity incidence during the first postnatal year.

Methods or Approach:
Babies were identified who were born at the University of Kansas Medical Center (KUMC) between mid-March 1973 through August 1975 and who were full-term, white, single births, with no evidence of congenital anomaly or intrauterine infection. Intended feeding mode by mother was noted. The babies who fit the criteria (followup in the KUMC Clinics for at least four visits in the first postnatal year with good documentation of dietary and infection history) were studied with regard to maternal age, socioeconomic status, educational level, smoking habits, other maternal factors, number of siblings, as well as feeding mode and duration of breastfeeding. Incidence of infection in the first year was correlated with all of these factors.
Results to Date:
There were 251 babies who fit all criteria; 127 mothers intended to breast feed while 124 intended to formula feed. Utilizing t-test on variables of these two groups, statistically significant differences showed that mothers intending to breast feed were older than those intending to formula feed, had more years of education, longer prenatal care, were less likely to smoke or be in the welfare hospital classification. The correlation matrix revealed that maternal education was the variable most significantly inversely correlated with infection ($p<0.0001$) and was the first to enter the regression equation. Its statistical significance persisted in the presence of other added factors. Although increased duration of breast feeding was also inversely correlated with incidence of infections, when this variable was coupled with maternal educational categories utilizing the t-test, there were no significant differences in number of infections between babies who were formula fed and those fed breast milk for a short period (≤ 3 months) or a longer period (>3 months). Maternal education appeared to have played a highly significant role in the health of the children studied. The feeding mode itself constitutes only one of many choices which a mother makes in the total care of her child. Obviously, other maternal variables, including cigarette smoking and length of prenatal care, are part of the total number of choices available to mothers.
Project Dates:
February 1979–1982.
Financial Support:
Mead Johnson and Company.
Reference:
Holmes, G.E.; Hassanein, K.M.; Miller H.C. "Factors Associated With Morbidity Among Breast Fed and Formula Fed Babies." *Pediatrics* 72(3):300-306, September 1983.

0879. UNIVERSITY OF KANSAS, COLLEGE OF HEALTH SCIENCES AND HOSPITAL, Building 48, Room 154, Rainbow Boulevard at 39th Street, Kansas City, Kansas 66103.

Project Title:
Anal Cancer in Women: Etiologic Factors.
Principal Investigators:
Holmes, F.F.; Holmes, G.E.
Objective:
To identify possible etiologic factors in anal cancer by utilizing an interview instrument covering demographic data, previous disease, occupation and workplace, tobacco, alcohol, and drug use, and obstetric and gynecologic history of women.
Methods or Approach:
The questionnaire is being administered to female cases and controls. Blood is drawn from each subject for testing to ascertain prevalence of HSV-1 and HSV-2, FTA, and HPV. Interviews are conducted face to face. Controls are obtained by a method of random digit dialing, focused to the first three digits (exchanges) of cases' telephone numbers.
Results to Date:
Interviews are being conducted, but results are not yet available.
Project Dates:
September 1983–August 1986.
Financial Support:
NCI (NIH-NCI-DCCP).

0880. WASHBURN UNIVERSITY, Topeka, Kansas 66621.

Project Title:
A University Campus Smoking and Health Fair.

Principal Investigators:
Evans, R.; Decker, B.
Objective:
To (1) stage a 2-day health fair aimed specifically at tobacco use; (2) evaluate the impact of the fair on those who attended; and (3) focus attention on the university as a worksite, where students, faculty, and staff need to learn more about smoking hazards and resources for cessation.
Methods or Approach:
The fair will include exhibits, booths, films, and health assessments by local groups, including the American Lung Association, the American Heart Association, and the American Cancer Society. Pulmonary function and other health testing will be conducted by two local hospitals and students in a university respiratory therapy program. Kansans for Nonsmokers' Rights and the Kansas Department of Health will also participate. Those who attend will be asked to complete questionnaires and will be interviewed at random to determine what was learned.
Results to Date:
Project is in a preliminary phase.
Project Dates:
September 1984–March 1985.
Financial Support:
Washburn University.

0881. USDA, AGRICULTURAL RESEARCH SERVICE, Lexington, Kentucky 40506.

Project Title:
Reduce Hazardous Compounds in Tobacco Leaf and Smoke by Chemical, Physical, and Biological Methods.

Principal Investigators:
Lowe, R.H.; Hamilton, J.L.; Andersen, R.A.
Objective:
To develop technology for reducing or eliminating hazardous compounds by altering the biological and chemical processes that occur during senescence and curing.
Methods or Approach:
Biochemical properties of tobacco processed by different curing methods, the interrelationships between the phytochemistry of tobacco components, and the relation of senescence and curing processes to these components will be studied. Biosynthetic pathways and enzyme systems involved in formation and metabolism of hazardous compounds will be determined, and ways will be developed to reduce or eliminate them through biochemical changes and modified curing procedures, such as extraction of compounds during homogenized leaf curing or alteration of the biological changes by controlled bulk-curing techniques. Chemical components will include nitrosamines, proteins, nitrated alkaloids and related nitrogen compounds, plant phenolics, tar, waxes, lipids, and related compounds.
Results to Date:
Reduction of lamina NO_3 to NO_2 during curing provides a substrate for formation of tobacco-specific nitrosamines from alkaloid-derived amines. The role of microorganisms, curing methods, and environment, and simulated aging of cured tobacco on biological and chemical changes were determined. Homogenized leaf curing (HLC) resulted in increases in bacteria capable of NO_3 reduction to NO_2, decreases in NO_3 and nicotine, and increases in NO_2 and N-nitrosonornicotine. Antibiotics inhibited reduction of NO_3 in HLC. Addition of denitrifiers to HLC and adjustment to pH 9 resulted in complete removal of NO_3 and limited accumulation of NO_2. Simulated aging of HLC resulted in a gradual but marked decrease in NO_2, and a slight decrease in total alkaloids, with nornicotine decreasing more than the other alkaloids. In contrast, aged air-cured tobacco had increases in NO_2 and decreases in NO_3, nicotine, and nornicotine. During air-curing, no changes in NO_3 or NO_3-reducing bacteria were detected during the first 18 days. Three days later, during the onset of lamina browning and cellular disruption, NO_3-reducing bacteria increased markedly and NO_2 increased from trace amounts to over 800 μg/g of leaf.
Project Dates:
October 1979–October 1984.
Financial Support:
USDA (6430-20882-002D).
References:
(1) Andersen, R.A.; Oh, J.H.; Kasperbauer, M.J. "Formation of N-Nitrosonornicotine in Burley Tobacco Materials During Curing and Storage in Controlled Environments." *Proceedings of the American Association for Cancer Research*, 1982. (2) Andersen, R.A.; Kasperbauer, M.J. "Alkaloids and Other Nitrogenous Constituents in Burley Tobacco: Influence of Post-Harvest Treatment, Symposium on Chemistry of Tobacco and Tobacco Smoke." *Agricultural Food Chemistry*, 1982. (3) Andersen, R.A.; Kasperbauer, M.J. *Alkaloids and Other Nitrogenous Constituents in Burley Tobacco. Influence of Post-Harvest Treatment.* 94th Report, Kentucky Agricultural Experiment Station, 1982. (4) Andersen, R.A.; Kasperbauer, M.J.; Burton, H.R., et al. "Changes in Chemical Composition of Homogenized Leaf-Cured and Air-Cured Burley Tobacco Stored in Controlled Environments." *Journal of Agricultural Food Chemistry* 30(4):663-688, July-August 1982. (5) Hamilton, J.L.; Lowe, R.H. "Use of Water Absorbent Polymer in Tobacco Seedling Production and Transplanting." *Tobacco Science* 26:17-20, 1982.

0882. USDA, AGRICULTURAL RESEARCH SERVICE, Department of Agricultural Engineering, Lexington, Kentucky 40506.

Project Title:
Preparation, Storage, and Marketing Burley Tobacco to Prevent Formation of Mycotoxins.

Principal Investigators:
Henson, W.H.; Yoder, E.E.
Objective:
To develop methods and equipment for removing cured leaves from stalks, leaf packaging, storage, and handling through market that may be used by all tobacco growers to reduce labor, reduce hazardous constituents in the leaf and smoke, and increase quality and consumer safety.
Methods or Approach:
Alternatives for market preparation, leaf packaging, and materials handling for applicability to all major tobacco markets were analyzed, and effects of environmental conditions during farm storage on the quality of tobacco were evaluated. Variables to be considered included tobacco form, density, type of package, weather conditions, and length of storage in design of equipment for market preparation, packaging, and handling of tobacco. Nondestructive methods for leaf moisture testing as an aid to orderly marketing, reducing harmful effects of high-moisture tobacco, and reducing fossil fuel inputs needed for excess moisture removal processing were evaluated.
Results to Date:
Control and power pneumatic circuitry has been designed for an experimental machine capable of automatic high-capacity stripping, grading, and baling of intact tobacco leaves. A laboratory device is being constructed to test the stripping component, regarded as the most crucial problem.
Future Plans:
The leaf stripping component and sliced leaf market preparation procedures will be tested during 1984-85.
Project Dates:
May 1968–May 1983.
Financial Support:
USDA (6430-20881-005D).
References:
(1) Henson, W.H., Jr.; Bunn, J.M.; Walton, L.R. "Electrical Measurement of the Moisture Content of Burley Tobacco." *Tobacco Science* 28:78-84, June 22, 1984. (2) Henson, W.H., Jr.; Nickell, W.T.; Duncan, G.A. "Measuring the Moisture Content of Cured Burley Tobacco With a Commercially Available Dielectric Meter." *Tobacco Science* 28:102-109, August 24, 1984. (3) Nickell, W.T.; Henson, W.H., Jr. "A Two-Frequency Tank Circuit Moisture Meter for Burley Tobacco." *Tobacco Science* 28: August 1984.

0883. USDA, AGRICULTURAL RESEARCH SERVICE, Lexington, Kentucky 40506.

Project Title:
Improved Tobacco Safety by Genetic Modifications and Reduced Pesticide Residues Via Host Resistance.

Principal Investigators:
Litton, P.D.; Kasperbauer, M.J.

Objective:
To (1) investigate new procedures and apply most effective methods for development of plants with reduced levels of undesirable chemical constituents; (2) determine mode of inheritance of chemical traits; (3) develop host resistance in air- and fire-cured types to circumvent use of chemicals that produce residues on leaf and in smoke.

Methods or Approach:
Comprehensive experiments will be conducted, including evaluation of germplasm, intra- and interspecific transfer of desirable factors for pest resistance, and varying levels of chemical constituents that may be important in smoking and health. Crosses, disease screening, chemical analyses, statistical procedures, anther-derived haploids, and double haploids will be utilized. New lines will be characterized for host resistance and chemical composition.

Results to Date:
Advancement and testing of burley and dark tobacco breeding lines possessing genetic resistance to as many as seven diseases was continued. Segregating populations were screened by artificially inoculating in the greenhouse and field or by selecting for resistance in disease-infested nursery plots. S(4)BC(6) and S(5)BC(5) burley lines carrying resistance to five diseases and the TI 1406 resistance to tobacco etch and tobacco vein mottling virus were tested for yield, quality, agronomic characteristics and chemical composition in replicated plots at three locations. Promising lines of dark air- and fire-cured tobacco were evaluated in replicated plots and in several on-farm tests in the dark tobacco production areas. A manuscript was prepared on comparison of growth and developmental characteristics of doubled haploids vs. highly inbred burley cultivars. Doubled haploids flowered later and developed smaller plants that produced less cured leaf with lower alkaloid content than did the inbreds. Some developmental differences were found among doubled haploids from a given inbred plant, and from second cycle doubled haploids from a given doubled haploid. Differences among doubled haploid lines originating from different microspores from the same inbred plant were attributed to residual heterozygosity and mutations, while those among second cycle doubled haploid lines originating from the same doubled haploid were attributed to mutations.

Project Dates:
October 1979–October 1984.

Financial Support:
USDA (6430-20882-003D).

References:
(1) Kasperbauer, M.J.; Legg, P.D.; Sutton, T.G. "Growth, Development and Alkaloid Content of Doubled Haploids vs. Inbreds of Burley Tobacco." *Crop Science*, (In press). (2) Litton, C.C. "Survival of *Thielaviopsis basicola* in Naturally Infested Tobacco and in Pure Culture." *Tobacco Sciences* 26:94-97, 1982. (3) Nielsen, M.T.; Litton, C.C.; Calvert, J., et al. "Kentucky Official Burley Tobacco Variety Test." Progress Report No. 261, Kentucky Agricultural Experiment Station, 1982.

0884. USDA, AGRICULTURAL RESEARCH SERVICE, Lexington, Kentucky 40506.

Project Title:
Homogenized Burley Tobacco Curing to Reduce Hazardous Substances.

Principal Investigator:
Yoder, E.E.

Objective:
To (1) develop a highly mechanized burley tobacco production system having capacity for precise quality control; (2) determine specifications for equipment and procedures to grow, harvest, grind, incubate, dry, and handle burley tobacco for a homogenized curing process; and (3) determine effects of processing variables on health-related properties.

Methods or Approach:
Experimental and pilot processing equipment such as defoliators, high-shear grinders, pumps, blowers, sparged-mixers, dewaterers, driers, and heat exchangers will be designed, selected, and operated. Physical properties of green and incubated tobacco slurries, such as viscosity, thermal conductivity, fiber structure, and coefficients for gas diffusion and forced convection will be determined. Product quality will be evaluated by chemical analyses and bioassay. An engineering analysis of the system will be conducted from the standpoint of materials handling and system economics.

Results to Date:
Tobacco of three genetic lines (Ky-14, High Alkaloid B-21, and nornicotine converter) were incubated with and without ascorbic acid additive during levels of incubation, with the duration ranging from 0 to 25 hours. Concentrations of alkaloids, nitrates, nitrites, amino-free acids and protein extractables in the homogenized leaf cured tobacco were reduced during storage. Concentrations of N-nitrosonornicotine increased during storage. Rate and magnitude of component change was directly proportional to change in incubation temperature. A laboratory procedure for controlling the size and shape of ducts in the experimental cigarette combustion temperature and gas discharge has not yet been developed.

Project Dates:
March 1975–February 1987.

Financial Support:
USDA (6430-20881-001D).

Reference:
Anderson, R.M.; Kasperbauer, M.J.; Burton, H.R., et al. "Changes in Chemical Composition of HLC and Air-Cured Burley Tobacco Stored in Controlled Environment." *Journal of Agricultural and Food Chemistry* 30:663-668, 1982.

0885. KENTUCKY STATE UNIVERSITY, Community Research Service, Frankfort, Kentucky 40601.

Project Title:
Obesity Among Selected Elderly Females In Central Kentucky: An Approach to Its Evaluation.

Principal Investigators:
Lee, C.J.; Panemangalore, M.

Objective:
To identify differences between obese and nonobese individuals in eating patterns, nutritive intakes, and health problems; determine factors associated with obesity.

Methods or Approach:
Dietary, biochemical, and clinical evaluations were conducted on 130 elderly obese and nonobese women in central Kentucky. Correlation coefficients, t-tests, and multiple regression techniques were employed to detect effects of socioeconomic

factors, dietary intake, lifestyle, and physical activity on anthropometric and metabolic parameters.

Results to Date:

Although there was no significant difference in total caloric intake between smokers and nonsmokers, smokers had significantly lower triceps and subscapular skin folds and buttocks circumference ($p<0.05$), and consumed significantly fewer fruits and vegetables ($p<0.05$) than nonsmokers. The most pronounced differences between smokers and nonsmokers were observed in hematological parameters; smokers had significantly elevated values in leukocyte and erythrocyte counts, hematocrit, and hemoglobin ($p<0.001$).

Project Dates:

May 1980–May 1985.

Financial Support:

USDA, Cooperative State Research Service.

0886. UNIVERSITY OF KENTUCKY MEDICAL CENTER, MS 681, Division of Hematology/Oncology, 800 Rose Street, Lexington, Kentucky 40536.

Project Title:

The Effect of Cigarette Smoking on Bone Marrow Production of Inflammatory Cells and Their Precursor Stem Cells.

Principal Investigator:

Doukas, M.

Objective:

To determine if the increase in peripheral blood granulocyte count and increase in lung granulocytes and macrophages in smokers is related to increased production by bone marrow in response to a hormonal signal produced by lung tissue of smokers in response to low grade inflammation.

Methods or Approach:

Experiments will investigate in vivo effects of cigarette smoking or defined tobacco constituents on murine marrow proliferation to (1) ascertain marrow cellularity, percentage of marrow cells committed to leukocyte production, and marrow content of white cell progenitor; and (2) ascertain effect of smoking on capacity of host mice to stimulate normal marrow cells to proliferate within diffusion chambers implanted intraperitoneally during and after smoke exposures. Experiments will also determine changes induced by smoking on levels of granulocyte/macrophage colony stimulating activity (GM-CSA) by measuring (1) serum GM-CSA levels in smoked and control animals after varied (6 to 12 weeks) smoking exposures; and (2) ascertain production of GM-CSA by lung tissue from smoke-exposed mice and appropriate control animals.

Results to Date:

Examination of peripheral blood at week 6 and week 9 showed no significant alteration in white cell count, hematocrit, and differentials between control, sham, and both 2R1 and 2A1 smoke-exposed animals. This is not unexpected as the peripheral white cell count is an insensitive measure of marrow production of inflammatory cells. However, data from week 6 of bone marrow cellularity and stem cell pools have revealed significant elevations in these parameters in smoke-exposed animals compared with controls.

Future Plans:

Research will include in vitro exposure of normal marrow precursors to defined tobacco products and examination of the proliferative response of such precursors and function of their differentiated progeny (granulocytes/macrophages).

Project Dates:

July 1984–July 1985.

Financial Support:

KTHRI; KTRB (124-05-7H350-4A035).

0887. UNIVERSITY OF KENTUCKY, COLLEGE OF MEDICINE, Division of Cardiovascular Medicine, Lexington, Kentucky 40536.

Project Title:

Effects of Cigarette Smoking on Regional Coronary Hemodynamics and Metabolism.

Principal Investigators:

Booth, D.C.; DeMaria, A.N.

Objective:

To (1) determine the influence of cigarette smoking upon coronary blood flow, coronary vascular resistance, and regional coronary metabolism; (2) reassess the effect of cigarette smoking upon systemic hemodynamics; (3) determine whether or not cigarette smoking can be implicated in the genesis of coronary artery spasm in patients with coronary artery disease; and (4) determine whether or not any of these responses differ between normal individuals and patients with coronary artery disease.

Methods or Approach:

The influence of cigarette smoking upon coronary blood flow will be assessed using the coronary sinus thermal dilution technique. Patients undergoing cardiac catheterization at the University of Kentucky Medical Center or at Lexington Veterans Administration Medical Center will be candidates for the study, which will take place following completion of diagnostic cardiac catheterization. A triple thermistor catheter will be used for coronary sinus flow determination, to estimate anterior myocardial and inferior myocardial flow. Blood samples will also be taken for determination of carbon monoxide and nicotine concentration, as well as for determination of arterial and coronary sinus lactate. To assess whether or not smoking can be implicated in coronary artery spasm, cold pressor tests will be performed before and following cigarette smoking.

Results to Date:

Data suggest that smoking results in a mild increase in coronary vascular resistance.

Project Dates:

June 1982–1983.

Financial Support:

KTHRI (124-05-7H350-5B510).

0888. UNIVERSITY OF KENTUCKY, COLLEGE OF MEDICINE, Division of Cardiovascular Medicine, Lexington, Kentucky 40536.

Project Title:

Noninvasive Evaluation of the Effects of Cigarette Smoking Upon Cardiac Size and Function in Patients With Coronary Artery Disease.

Principal Investigator:

DeMaria, A.N.

Objective:

To (1) evaluate left ventricular contractile pattern by means of noninvasive techniques; (2) provide information regarding the response of left ventricular size, ejection fraction, and regional contractile pattern to cigarette smoking; (3) discern any potential differences in the response of normally vs. abnormally perfused ventricular myocardium to cigarette smoke; and (4) determine a baseline for assessing potential therapeutic interventions.

Methods or Approach:

Noninvasive studies will be performed in normal control subjects, as well as in patients with coronary artery disease. Two-dimensional echocardiographic imaging and pulsed Doppler velocity measurements will be performed prior to and following the consumption of two cigarettes. Echocardiograms will be obtained in the long and short axis parasternal projections, as well as in the apical and subcostal views with either a mechanical or phased-array device. Doppler velocity measurements will be obtained in the ascending aorta from either the suprasternal notch or cardiac apex, or in the pulmonary artery from the parasternal area. Measurements to be made will include volumes, ejection fraction, regional endocardial motion, and velocity of contraction of the left ventricle by echocardiography. Doppler recordings will yield values for maximal velocity of aortic blood flow, time to peak velocity, and acceleration.

Results to Date:
Data indicate that smoking two cigarettes does not induce any significant changes in either left ventricular size or contractile performance.

Future Plans:
Having defined the response of cardiac size and performance to smoking, the composition of the cigarettes will be altered to determine which constituents of smoke are responsible for the induced changes.

Project Dates:
January 1982–December 1982.

Financial Support:
KTHRI (124-05-7H350-5B511).

0889. UNIVERSITY OF KENTUCKY, Department of Entomology, Lexington, Kentucky 40546.

Project Title:
Influence of Smoking on Biochemical Defense Mechanisms.

Principal Investigator:
Dorough, H.W.

Objective:
To determine the effect of smoking on biochemical reactions responsible for detoxification of xenobiotics that may induce toxicity or disease in man, and to assess the synergistic and antagonistic effects of other chemical exposures (pesticides, drugs, etc.) on smoke-induced modification of biodetoxification mechanisms.

Methods or Approach:
Adult male rats were exposed nose-only to cigarette smoke daily for up to 6 months. Exposure was confirmed by monitoring urinary concentrations and levels of carboxyhemoglobin in blood. After various intervals (months) of smoking, animals were assayed for in vivo and in vitro metabolic activities. Biochemical reactions evaluated included a series of Phase I reactions and several Phase II or conjugation reactions. Phenobarbital sleep time and zoxazolamine paralysis time were used as physiological indicators of enzyme induction or inhibition. Since urine of human smokers contains mutagenic components, the urine of rats was tested in the Ames assay.

Results to Date:
Smoke exposure did not induce statistically significant alterations in hepatic enzyme activity when measured in vivo (metabolism of orally administered pesticides, phenobarbital sleep time, zoxozolamine paralysis time) or in vitro (oxidation, hydrolysis, glucuronidation, glutathion conjugation) compared with sham-exposed rats. However, both experimental and sham-exposed controls had higher hepatic enzyme activity than cage controls. Data suggest that the trauma of restraining the animals was too great for one to separate effects of smoking and stress. Rat urine appeared nonmutagenic in the Ames assay, but its bactericidial activity was much greater than human urine, so no definitive conclusions were drawn regarding its mutagenicity.

Future Plans:
April 1982–December 1982.

Financial Support:
University of Kentucky; KTHRI.

0890. UNIVERSITY OF KENTUCKY, TOBACCO AND HEALTH RESEARCH INSTITUTE, Cooper and Alumni Drives, Lexington, Kentucky 40536.

Project Title:
Factors Influencing the Alterations in Prostacyclin and Thromboxane Induced by Cigarette Smoke.

Principal Investigator:
Lubawy, W.C.

Objective:
To determine if cigarette smoke or its components alter the balance of prostacyclin and thromboxane produced in various tissues.

Methods or Approach:
Platelets, aortic rings, and intact lungs are isolated from rats exposed to cigarette smoke, sham smoking, or normal room controls without daily handling. Arachidonic acid metabolism is examined in tissues using ^{14}C-arachidonic acid and radioimmunoassay. Intact lungs are also preloaded with ^{14}C-arachidonic acid and ventilated with whole smoke or the gas phase of smoke. Efflux of arachidonic acid metabolites is monitored.

Results to Date:
Chronic exposure to whole mainstream smoke decreases aortic conversion of ^{14}C-arachidonic acid to prostacyclin (PGI_2), increases platelet conversion to thromboxane (TXA_2), and lowers PGI_2/TXA_2 ratio in lung homogenates.

Future Plans:
Further experiments will be conducted to determine what factors in tobacco smoke contribute to the baseline PGI_2/TXA_2 alterations seen in animals chronically exposed to smoke.

Project Dates:
July 1984–June 1987.

Financial Support:
KTRB (4B006).

Reference:
Lubawy, W.C. "Factors Influencing the Alterations in Prostacyclin and Thromboxane Induced by Cigarette Smoke. *Life Sciences* 33:577, 1983.

0891. UNIVERSITY OF KENTUCKY, Department of Plant Pathology, Lexington, Kentucky 40546.

Project Title:
Relation of Enzymatic Activities With Quantities of Smoking and Health Related Tobacco Leaf Constituents During Air-Curing.

Principal Investigators:
Sheen, S.J.; Hamilton, J.L.

Objective:
To (1) study changes in activity of oxidases and hydrolases in burley tobacco under different conditions of air curing; (2) correlate enzymatic activities with accumulation of chemical constituents in air-cured leaves; and (3) compare enzymatic activities and leaf chemical constituents in virus-infected and healthy tobacco leaves before, during, and after air curing.

Methods or Approach:
Tobacco cultivar Ky 14 was air cured in three chambers regulating the following sets of temperature and humidity: 24°

C and 70 percent humidity; 32° C and 83 percent; and 15° C and 51 percent. Leaf samples taken during curing were analyzed for oxidase and hydrolase activity and chemical constituents. In a second experiment, the same enzymes and chemical constituents in the leaf of Virgin A, Ky 14, Va 509, and Selection 11A-2 (which differ in resistance to tobacco mosaic virus and tobacco etch virus) were studied during the course of conventional air curing. Results were statistically analyzed and inferred.

Results to Date:

Air curing under high temperature enhanced the activity of peroxidase, alkaline phosphatase, amylase, chlorophyllase, and protease. Polyphenoloxidase attained the highest activity in the low temperature environment. Positive correlation was obtained between chlorophyllase activity and the loss of plastid pigments. The quantitative change of nitrogenous compounds did not coincide with any enzymatic activity under investigation. Total hydrocarbons showed a similar level of concentration among the curing treatments. Virus-resistant tobaccos were generally low in polyphenoloxidase but high in chlorophyllase and alkaline phosphatase activity during air curing. Differences in peroxidase activity among the resistant and susceptible genotypes were not significant. Changes in leaf chemistry cannot be correlated with enzymatic activity in most cases nor with genotypes for virus resistance and susceptibility, possibly because of the complexity of catabolic processes in tobacco leaf and the nonspecificity of leaf enzymes under investigation.

Project Dates:

July 1982–December 1983.

Financial Support:

USDA (58-7B30-2-413).

0892. UNIVERSITY OF KENTUCKY, Department of Physiology, Lexington, Kentucky 40536.

Project Title:

Chemosensitivity of the Crayfish Slowly Adapting Stretch Receptor to Nicotine.

Principal Investigators:

Taylor, R.F.; Frazier, D.T.

Objective:

To characterize the chemosensitive component of mechanoreceptors using the isolated crayfish muscle receptor organ.

Methods or Approach:

It has previously been demonstrated that slowly adapting respiratory stretch receptors in the anesthesized dog are stimulated by cigarette smoke and nicotine aerosol. This stimulation has two components: an indirect effect of nicotine on airway parasympathetic ganglia producing bronchoconstriction and subsequent stretch receptor activation, and a direct stimulatory effect of nicotine on the sensory receptor membrane. Crayfish muscle, which is not sensitive to nicotine or acetylcholine, enabled testing for any direct effects of nicotine on the receptor membrane. A single, slowly adapting stretch receptor in the tail of the crayfish was recorded using extracellular recording methods. The stretch receptor was surgically isolated, bathed in van Harreveld's solution, and kept at 18° C. Single unit stretch receptor activity was recorded simultaneously with muscle tension in the tail segment. The firing behavior of the receptor was monitored under isotension in the presence of nicotine (0.07 μM) before and after treatment with hexamethonium (690 μM). The effect of nicotine on the sensitivity of the stretch receptors was tested in a second group of animals, with sensitivity defined by the slope of receptor activity as a function of changes in muscle tension, before and after treatment with hexamethonium.

Results to Date:

Under conditions of isotension, nicotine increased receptor activity fourfold to fivefold, a response that was totally abolished after treatment with hexamethonium. Hexamethonium alone had no effect on normal stretch receptor activity. Results from the second study showed a linear relationship between stretch activity and muscle tension and a significant increase in receptor sensitivity after nicotine treatment that was abolished after treatment with hexamethonium. Results demonstrate that nicotine directly stimulates the slowly adapting stretch receptor independent of any changes in muscle tension. Also, the sensitivity of the receptor response to changes in muscle tension was significantly increased, indicating that the transducing process was altered. The ability of hexamethonium to totally block the stimulation effects of nicotine without interfering with the normal transduction process indicates the possibility of nicotinic receptors located somewhere on the sensory receptor membrane.

Future Plans:

Further investigation of the mechanoreceptor membrane events associated with the presence of nicotine will be conducted using intracellular electrodes to record changes in ionic conductances that might underlie such pharmacological effects.

Project Dates:

July 1984–June 1985.

Financial Support:

KTHRI (4A024).

0893. UNIVERSITY OF KENTUCKY, Department of Physiology and Biophysics, MS-507 Chandler Medical Center, Lexington, Kentucky 40536-0084.

Project Title:

Response of Airway Receptors to Cigarette Smoke and Nicotine Aerosols.

Principal Investigators:

Frazier, D.T.; Lee, L.-Y.; Taylor, R.T.

Objective:

To (1) demonstrate that cigarette smoke with varying nicotine levels has similar effects on slowly adapting respiratory stretch receptors (SARSR); (2) determine effect of tobacco smoke and nicotine aerosols on rapidly adapting airway receptors; and (3) develop an isolated upper airway preparation for studying effects of tobacco smoke on receptors.

Methods or Approach:

A cigarette smoke generating machine is placed in series with a respirator so that smoke (10 percent in 750 mL of air) is drawn into the respirator and pumped directly into the tracheal cannula of anesthetized and paralyzed dogs. A second respirator (in parallel with the first), allows for ventilation of the animal during the control period with air not contaminated with smoke. An attempt is made to filter air in the room with an air cleaner and to separate the intake and outflow of the two respirators from each other. The 750 mL smoke reservoir is emptied over the first, second, and third breaths. The smoke-filled respirator is in communication with the tracheal cannula for a total of five breaths. P_{tp}, V_E, and receptor activity is recorded on magnetic tape and stored for later analysis.

Results to Date:

In all instances, introduction of saline aerosols resulted in a decrease in P_{tp} and SARSR activity; 2 percent nicotine aerosols resulted in a significant increase in P_{tp} with a concomitant increase in SARSR spikes per burst. A significant portion of increased SARSR activity was sustained when nicotine-induced pressure changes were reduced by the presence of isoproterenol (i.v. or aerosol). A dose–response effect was demonstrated by varying the nicotine concentration from 1 percent to 8 percent. SARSRs above the carina demonstrated a greater response to nicotine than those below the carina. It was concluded that nicotine increases SARSR activity by increasing P_{tp} and receptor sensitivity in a dose-related manner. The receptor response may depend on the degree of distensibility of the supporting tissue and whether the local architecture promotes deposition. Both factors are related to the location of the receptor along the tracheobronchial tree.

Future Plans:

An isolated upper airway preparation will be developed to study effects of tobacco smoke and/or nicotine on airway receptors.

Project Dates:

July 1984–June 1985.

Financial Support:

KTHRI (124-05-7H750-4A024).

0894. UNIVERSITY OF KENTUCKY, TOBACCO AND HEALTH RESEARCH INSTITUTE, Lexington, Kentucky 40546-0236.

Project Title:

Improvement and Monitoring of Smoke Generating, Manipulating, and Exposure Systems.

Principal Investigator:

Griffith, R.B.

Objective:

To continue development, improvement, and testing of equipment and procedures for smoke generation, manipulation, and monitoring in in vitro and in vivo exposure systems; assist investigators in use of the equipment and procedures.

Methods or Approach:

Further improvements in equipment and procedures for various smoke exposure systems will be made, with emphasis on validating the relatively simple monitoring procedures already developed. Routine monitoring of the results from the University of Kentucky Tobacco and Health Research Institute research program provides guidance for identifying improvements needed and assistance to research investigators.

Results to Date:

Smoke exposure systems for simultaneous exposure of experimental animals, perfused lungs, or cell cultures to mainstream and sidestream smoke from the same cigarette have been developed. All smoke generation, manipulation, and exposure variables can be controlled and studied, and use of the same kind of smoke in different smoke exposure systems increases chances of correlating results. Results from cell culture studies can be used for guidance for more time-consuming, expensive in vivo animal exposure studies. Development of a computer program for characterizing human smoking behavior permits a definition of smoke generation parameters of possible importance in animal studies.

Future Plans:

Validation of present monitoring procedures and improvements in animal restraint procedures will be areas of particular concern.

Project Dates:

July 1984–June 1985.

Financial Support:

KTHRI (10023).

0895. UNIVERSITY OF KENTUCKY, Department of Anatomy, Lexington, Kentucky 41536.

Project Title:

Pulmonary Tissue Response to Chronic Smoke Exposure in Young and Old Mice. I. Lung Morphology and Function.

Principal Investigator:

Matulionis, D.H.

Objective:

To determine whether prolonged smoke inhalation results in pulmonary abnormalities that can be attributed to smoke alone; assess the contribution of the aging process to the manifestation of lung pathology following chronic cigarette smoke inhalation.

Methods or Approach:

The effects of long-term cigarette smoke inhalation were assessed in lungs of C57Bl/6 young and old mice. Smoke exposure occurred twice/day over a 9-month period, beginning when young animals were 2 months old and old animals were 8 to 11 months old. Structural changes of lung tissue were evaluated using light and electron microscopy and quantified via morphometric procedures. Lung volume, lung elastic recoil (compliance change), diffusing capacity, and diffusing capacity per unit volume of lung were determined using standard procedures.

Results to Date:

Examination of pulmonary tissue revealed peribronchiolar and perivascular accumulations of lymphocytes and macrophages in lungs of both young and old smoke-exposed mice. Lesions were not observed in sham-treated or control animals of either age. Three anomalous manifestations, prominent only in smoke-exposed old animals, were (1) reduction of alveolar space with a concomitant increase in lung cellularity and thickened alveolar septa; (2) intra-alveolar accumulation of surfactant-like material; and (3) decreased pulmonary function. Pulmonary function data complemented morphologic and morphometric observations and indicated that the manifestation of abnormality noted in old smoke-exposed animals were restrictive in nature and conformed most closely to pulmonary fibrosis.

Future Plans:

Research is planned to assess the onset, progression, and end stage of pulmonary fibrosis following cigarette smoke inhalation.

Project Dates:

July 1983–June 1984.

Financial Support:

KTHRI (124-15-7H111-4A117).

0896. UNIVERSITY OF KENTUCKY, Department of Anatomy, Lexington, Kentucky 41536.

Project Title:

Pulmonary Tissue Response to Chronic Smoke Exposure in Young and Old Mice. II. Pulmonary Macrophage Response.

Principal Investigator:

Matulionis, D.H.

Objective:

To provide data from chronically smoke-exposed young and old mice on population size, dimensions, and subcellular alterations of pulmonary macrophages.

Methods or Approach:

Using quantitative procedures, the effects of chronic cigarette smoke inhalation (9 months) on the population size, cell dimensions, and ultrastructure of in situ pulmonary macrophages of young (2 months old) and old (8 to 11 months old)

C57BL/6 mice were assessed. Light microscopic preparations of lung were used to quantify the number of pulmonary macrophages (septal and alveolar) per unit area of pulmonary tissue that represented a fraction of the total population size. Tissues prepared for electron microscopy were used to quantify (morphometrically and/or algorithmically) mean diameter and area of phagocytes and volume fractions, surface volume, numerical density, and mean volumes of major cytoplasmic organelles. Data were evaluated statistically.

Results to Date:

Chronic smoke exposure significantly elevates pulmonary macrophage population size over control values; however, the number of phagocytes was more than three times higher in young mice than in old mice. The mean area and diameter of macrophages in young and old smoke-exposed animals were significantly larger than in controls. Morphometric data indicate that enlargement in old animals was due to increased numbers and size of secondary lysosomes and accumulation of inclusions resembling crystalline kaolinite within the cells. More than 1 percent of cell volume was occupied by this material. Evaluation of dimensional changes of organelles involved in synthesis and metabolism suggests that smoke inhalation has no effect on or slightly depresses these activities. It is speculated that decreased macrophage population size in lungs of old smoke-exposed mice, altered lysosomal system, and accumulated inorganic crystalline material may be related to development of pulmonary fibrosis.

Future Plans:

Further research will assess the involvement of the inorganic particulates in cigarette smoke and the significance of reduced pulmonary macrophage population in the development of lung fibrosis.

Project Dates:

July 1983–July 1984.

Financial Support:

KTHRI (124-15-7H111-4117).

0897. UNIVERSITY OF KENTUCKY, MEDICAL CENTER, Department of Behavioral Science, Lexington, Kentucky 40536-0086.

Project Title:

Individual Variability in Sensitivity to Nicotine.

Principal Investigator:

Jones, R.A.

Objective:

To establish the stability of individual differences in nicotine sensitivity over time; examine personality correlates of differential nicotine sensitivity.

Methods or Approach:

Utilizing increases in pulse rate as an indicator of nicotine sensitivity, the research seeks to document the stability of responsiveness to nicotine at varying callback intervals for both male and female subjects. During initial tests for nicotine sensitivity, subjects' pulse rates were monitored continuously for 5 minutes prior to, 5 minutes during, and 5 minutes immediately following smoking. Twenty subjects of each sex were then selected from a larger group of 120, on the basis of high (pulse rate increased >9 beats/min in first 5 min of smoking) or low (<9 beats/min) responsiveness. Retests, conducted at intervals varying from 1 week to 4 months, included puff analysis and the completion of several personality scales.

Results to Date:

Retests of the initial high and low sensitivity groups revealed that the two groups maintained the respective levels of pulse responsiveness to nicotine over time. Subjects who were physiologically aroused by smoking, as indicated by increased heart rate, did not differ from those less responsive to nicotine in terms of extraversion scores on the Eysenck Personality Inventory (Form B); however, subjects experiencing physiological arousal as a result of smoking one cigarette (1.57 mg/nicotine) were significantly more neurotic than subjects not experiencing such arousal ($p=0.001$). This was true for both males and females considered separately. In addition, it was found that respiratory rate decreased slightly while smoking, because smokers took deeper breaths while smoking. It is suggested that this later finding may have implications for Nesbitt's Paradox: subjects' perception that smoking calms them while it is actually stimulating.

Future Plans:

The hypothesis that variations in diet, specifically the acid-producing properties of ingested foods, will influence sensitivity to the physiological and psychological effects of nicotine will be tested.

Project Dates:

January 1984–December 1984.

Financial Support:

KTHRI (5D523).

0898. UNIVERSITY OF KENTUCKY, Department of Agronomy, Lexington, Kentucky 40546-00914.

Project Title:

Identify and Reduce Chemical Precursors in Tobacco That Form Hazardous Constituents in Smoke.

Principal Investigators:

Andersen, R.; Kasperbauer, M.; Leggett, J.E., et al.

Objective:

To improve tobacco safety through the use of new chemical, physical, and applied science procedures to reduce or remove constituents from tobacco leaf or smoke that are potentially hazardous to the consumer.

Methods or Approach:

Tobacco samples derived from tobacco grown according to varied genetic, physiological, curing, and agronomic parameters will be prepared using selected experimental, new, and standard production techniques. Quantitative chemical analysis of tobacco samples will be carried out after identification of health-related components and their precursors. Results of chemical analysis will be used to guide efforts to reduce hazardous constituents in tobacco by new production practices that minimize carcinogenic component accumulations.

Results to Date:

It was determined that N'-nitrosonornicotine (NNN) is formed in tobacco during new or standard production techniques that lead to increases in nitrite, nitrate, or nicotine-related alkaloids. Accumulations were also related to the genetic line of burley tobacco used in preparation of tobacco materials. The lowest increase in NNN occurred with a low-alkaloid isoline of burley tobacco; the highest increase occurred with a high nornicotine-nicotine line.

Future Plans:

Further research will determine effects of postharvest treatments of burley tobacco on accumulations of 4-(N-methyl-N-nitrosamino)-1-(3-pyridyl)-1-butanone.

Project Dates:

1980–1985.

Financial Support:

ARS.

0899. UNIVERSITY OF KENTUCKY, COLLEGE OF PHARMACY, Washington and Gladstone Streets, Lexington, Kentucky 40536-0053.

Project Title:
Influence of Smoking on Serum Protein Composition and the Protein Binding of Drugs.

Principal Investigators:
Benedek, I.H.; McNamara, P.; Blouin, P.
Objective:
To determine the influence of smoking on α_1-acid glycoprotein (α_1-AGP) and serum albumin concentrations and protein binding of phenytoin and propranolol in healthy subjects.
Methods or Approach:
Male volunteers (10 smokers and 10 nonsmokers) were free of disease or any medication known to cause changes in either serum α_1-AGP concentrations or drug binding to serum proteins. Venous blood samples, collected following an overnight fast, were allowed to clot at room temperature for 2 hours and were then centrifuged. Serum was collected and stored at -20° C. Serum protein binding was determined by equilibrium dialysis. Propranolol and phenytoin were added to achieve concentrations of 100 ng/mL and 15 µg/mL, respectively. Drug concentrations were quantitated by liquid scintillation counting. Statistical analyses were made using the student's t-test.
Results to Date:
Smokers tended to have lower serum albumin concentrations than nonsmokers; however, the difference was not statistically significant. Mean serum α_1-AGP concentrations were significantly increased in smokers, although the underlying mechanism(s) is unknown. The clinical significance appears to be small, but data suggest that the smoking status of an individual should be added to the growing list of factors that can alter serum α_1-AGP concentrations. Smoking status is a factor worth controlling when designing or evaluating serum protein binding studies.
Project Dates:
August 1981–July 1983.
Financial Support:
University of Kentucky.
Reference:
Benedek, I.H.; Blouin, R.A.; McNamara, P.J. "Influence of Smoking on Serum Protein Composition and the Protein Binding of Drugs." *Journal of Pharmacy and Pharmacology* 36:214-216, 1984.

0900. UNIVERSITY OF KENTUCKY, TOBACCO AND HEALTH RESEARCH INSTITUTE, Cooper and Alumni Drives, Lexington, Kentucky 40546-0236.

Project Title:
Toxicological Studies of the Relationship Between Cigarette Smoke and Pulmonary Emphysema.

Principal Investigator:
Diamond, L.
Objective:
To evaluate the pulmonary toxicity of smoke particulates and/or nicotine using an experimental animal model.
Methods or Approach:
Although the causal relationship between cigarette smoking and pulmonary emphysema is well established, the specific component or components in cigarette smoke responsible in pathogenesis are unknown. Recent evidence suggests that smoke particulates and/or nicotine may be involved in induction of emphysema. Three experiments will be conducted. The first compares functional and structural changes that occur in the lungs of rats on exposure to smoke from cigarettes that deliver significantly different quantities of particulates. Some of the animals are pretreated with an elastolytic enzyme (porcine pancreatic elastase, PPE) to render them more susceptible to the emphysema-inducing effects of cigarette smoke. In the second experiment, conducted in a similar manner, the smoke used is from cigarettes that deliver significantly different quantities of nicotine. The third experiment evaluates the ability of a synthetic peptidyl carbamate elastase inhibitor to prevent or ameliorate elastase-induced emphysema. In each experiment, an integrated sequence of pulmonary function tests, combined with morphometric analyses of lung tissue specimens, provides biological endpoints from which relative toxicities of the various interventions are evaluated.
Results to Date:
Preliminary data suggest that smoking can significantly enhance pulmonary tissue damage produced by a relatively low dose of PPE (400 IU/kg). This PPE dose produces moderate changes in pulmonary functions and morphometry; however, when combined with smoke exposure, it produces marked emphysematous changes.
Future Plans:
The hypothesis that smoking induces an imbalance between lung proteases and antiproteases that in turn promotes the development of pulmonary emphysema will be examined further.
Project Dates:
July 1984–June 1985.
Financial Support:
KTHRI.

0901. UNIVERSITY OF KENTUCKY, MEDICAL CENTER, Agricultural Science Center, Lexington, Kentucky 40536.

Project Title:
Genetic Engineering of Tobacco: Isolation of a Selectable Marker Gene for Use in Recombinant DNA Vectors.

Principal Investigators:
Dickson, R.C.; Collins, G.B.
Objective:
To (1) make tobacco resistant to tabtoxin, the causative agent of wildfire disease, and its analogue methionine sulfoximine (MSO) by introducing multiple copies of a glutamine synthetase (GS) gene into tobacco cells; (2) use a GS gene as a dominant selectable marker for plant recombinant DNA vectors; and (3) determine the molecular mechanism of the wildfire resistant gene of *Nicotiana longiflora*.
Methods or Approach:
Ti plasmids are being used to introduce genes into tobacco cells.
Results to Date:
Pilot experiments have shown that bacteria and yeast can be made resistant to MSO and tabtoxin by multiple copies of a GS gene.
Future Plans:
Multiple copies of a GS will be transformed into tobacco cells using a Ti plasmid. Transformed cells will be examined for resistance to MS and tabtoxin.
Project Dates:
January 1984–December 1985.
Financial Support:
KTHRI (124-05-7H180-5E526).

0902. UNIVERSITY OF KENTUCKY, COLLEGE OF PHARMACY, Washington and Gladstone Streets, Lexington, Kentucky 40536-0053.

Project Title:
Design and Synthesis of Specific Human Leukocyte Elastase Inhibitors.

Principal Investigators:
Digenis, G.A.; Agha, B.J.
Objective:
To utilize the carbamate functionality (ROCONR'R") in the design and synthesis of reversible, specific, active-site directed inhibitors of human leukocyte (HL) elastase.
Methods or Approach:
The proposed inhibitors are peptidyl carbamates where NR'R" is a polypeptide. This class of compound can provide specificity (peptide portion) and transfer a carbamoylating moiety to the active site of the enzyme. The effect of structural variations in R,R', and R" on the efficiency and duration of inhibition will be studied by testing against other serine proteases. The stability of promising inhibitors in blood and tissue homogenates will also be studied. The synthesis of peptidyl carbamates has already been developed. In vitro evaluation of the inhibitors toward HL elastase will be tested using the synthetic substrate MeO-Suc-Ala-Ala-Pro-Val-NA and monitoring the increase in absorbance at 410 nm. Ki values will be determined from Dixon Plots. The half-life of the promising carbamate esters in blood, lung, and liver homogenates will be measured spectrophotometrically or by a high performance liquid chromatographic method. In vivo work will be done on Long Evans rats, after inducing emphysema by intratracheal instillation of porcine pancreatic (PP) elastase. Inhibition will be given in divided doses and progress tested by conducting pulmonary function studies, lung morphometric evaluation, and examining pathologic abnormalities in the lung.
Results to Date:
More than 30 peptidyl carbamates have been synthesized and tested for inhibitory activity toward PP elastase, trypsin, chymotrypsin, and HL elastase; 20 were found to be good inhibitors of elastase without affecting the other serine proteases. Ki values varied from 4 to 42 μM. In vivo studies on emphysematous animals have been initiated.
Future Plans:
In vivo work to determine the potential of the inhibitors for treatment or prevention of emphysema will be continued. Toxicity of active inhibitors will be assessed and various drug delivery methods will be investigated. KTHRI (4A001).

0903. UNIVERSITY OF KENTUCKY, TOBACCO AND HEALTH RESEARCH INSTITUTE, Lexington, Kentucky 40546-0236.

Project Title:
Impact of Cigarette Smoke Exposure on the Pulmonary Cytotoxic Effector Cells in Mice.

Principal Investigator:
Gairola, C.
Objective:
To determine if exposure to cigarette smoke (mainstream) alters the cytolytic functions of various pulmonary effector cells.
Methods or Approach:
Pulmonary effector cells from control, sham-, and smoke-exposed mice will be obtained at different exposure points and in vitro cytolytic activity will be assayed using normal and tumor cells as targets. In vivo activity of the effector cells will be determined by comparing the extent of metastasis of tumor cells in control, sham- and smoke-exposed mice.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–December 1987.
Financial Support:
KTRB (5A533).

0904. UNIVERSITY OF KENTUCKY, Department of Physiology and Biophysics, Lexington, Kentucky 40503.

Project Title:
Influence of Chronic Tobacco Smoke Exposure on Cardiovascular Regulation.

Principal Investigators:
Bennett, C.H.; Richardson, D.R.
Objective:
To investigate influence of chronic tobacco smoke exposure on reflex regulation of arterial blood pressure.
Methods or Approach:
Male Sprague-Dawley rats were administered tobacco smoke for 6 to 8 months. Two groups of animals (A and B) received tobacco smoke containing different levels of nicotine: group A, high nicotine (4 mg/cigarette); group B, low nicotine (1 mg/cigarette). A third group (C) served as controls, receiving only puffs of room air. Reflex adjustments in mean arterial blood pressure (MAP), heart rate (HR), lower body blood flow, and lower body vascular resistance were compared between the groups.
Results to Date:
In the anesthetized control state, no significant difference existed for the cardiovascular parameters measured; however, perturbating the cardiovascular system by reducing central blood volume via a 60° head-up tilt elicited less decline in MAP in the two smoker groups than in controls; 23 percent in group A, 22 percent in group B, and 48 percent in group C (controls). Increasing MAP with phenylephrine elicited a significantly greater ($p < 0.05$) reduction in HR in groups A and B than in group C. Varying carotid sinus pressure elicited significantly greater changes ($p < 0.01$) in MAP in groups A and B than in controls. It is concluded that chronic tobacco smoke administration to laboratory rats increases the sensitivity of the reflex control of the cardiovascular system.
Project Dates:
September 1973–1981.
Financial Support:
KTHRI.
Reference:
Bennett, C.H.; Richardson, D.R. "Effects of Chronic Tobacco Smoke Exposure on Arterial Blood Pressure Regulation." *American Journal of Physiology* 247(Heart Circ. Physiol. 16): H556-H562, 1984.

0905. UNIVERSITY OF KENTUCKY, TOBACCO AND HEALTH RESEARCH INSTITUTE, Department of Oral Biology and Dentistry, Lexington, Kentucky 40536.

Project Title:
Cigarette Yield, Smoking History, and Smoking Behavior as Determinants of Smoke Exposure in Male Smokers.

Principal Investigators:
Bridges, R.B.; Humble, J.W.

Objective:
To determine the contribution of cigarette yield, smoking history, and smoking behavior to smoke exposure as measured by blood concentrations of thiocyanate, carboxyhemoglobin (COHb), nicotine, and cotinine.

Methods or Approach:
Male volunteers (170 smokers, 170 age-matched nonsmokers; mean age 35 years) completed a questionnaire concerning medical, pulmonary, drug, and smoking histories. Smokers were requested to smoke a cigarette of their usual brand, and smoking behavior (total duration and total volume) was determined using a cigarette-holder pneumotachograph. Venous blood was drawn 5 minutes after smoking and blood COHb, serum thiocyanate, and plasma nicotine and cotinine concentrations were determined. Relationships between indices of smoking behavior, cigarette consumption, or cigarette yield and blood concentrations of smoke constituents/metabolites were determined.

Results to Date:
Data suggest that cigarette consumption, cigarette yield, and smoking behavior are all important determinants of blood concentrations of smoke constituents/metabolites. However, to more completely explain blood concentrations, it may be necessary to take into account other factors that relate to absorption, including depth of inhalation. Data also suggest that smokers of low-yield cigarettes compensate by increasing puff number, mean puff volume, and total puff volume (but not the number of cigarettes smoked/day). However, smokers of extremely low-yield cigarettes appear to be unable to compensate completely to attain the same plasma cotinine concentrations.

Future Plans:
Experiments will be conducted to determine if measures of depth of inhalation increase prediction of blood concentrations of smoke constituents/metabolites.

Project Dates:
January 1982–December 1984. KTHRI.

0906. UNIVERSITY OF KENTUCKY, Departments of Oral Biology and Medicine, Lexington, Kentucky 40536.

Project Title:
Chronic Cigarette Smoking and the Concentration/Functional Activity of Serum Antiproteases.

Principal Investigators:
Bridges, R.B.; Wyatt, R.J.; Rehm, S.R.

Objective:
To determine if chronic cigarette smoking affects serum antiprotease levels and the total serum inhibitory activity against trypsin and elastase; determine the relationships of serum antiprotease concentrations or total protease inhibitory capacities and smoking history or pulmonary function.

Methods or Approach:
Fifty male smokers and an equal number of age-matched nonsmokers were characterized by smoking history, plasma nicotine and cotinine concentrations, and pulmonary function (i.e., forced expiratory spirometry and single breath nitrogen test). Serum samples were collected at 8 a.m., immediately after the smoking of one cigarette. Serum concentrations of alpha 1-protease inhibitor (α_1-PI) and alpha 2-macroglobulin (α_2-MG) were determined by radial immunodiffusion; total serum inhibitory capacities against trypsin and elastase were determined by generation of inhibitory curves constructed after addition of various amounts of serum.

Results to Date:
The relatively young smokers (31 years of age) exhibited only limited impairment of pulmonary function. Mean serum α_1-PI concentration was increased 13.3 percent in smokers, but α_2-MG concentrations appeared to be unaffected by smoking. The increase in serum α_1-PI concentration was accompanied by increases in total serum inhibitory capacities against trypsin (TIC, 9.9 percent) and elastase (EIC, 12.4 percent). Elevations of serum α_1-PI and total inhibitory capacities were significantly associated with increased pack years of smoking and plasma nicotine and cotinine concentrations. Although α_1-PI concentration did not correlate with any indices of pulmonary function, higher TIC and EIC were associated with tests of small airways dysfunction. Highly significant correlations were obtained between TIC and EIC and α_1-PI concentration in smokers and nonsmokers and linear relationships were not significantly different in the two populations. Thus, although chronic cigarette smoking increases serum α_1-PI concentration and total protease inhibitory capacities, there was no direct evidence to suggest that smoking affected functional activity of α_1-PI.

Future Plans:
Studies will determine if effects of smoking on functional activity of serum antiproteases are observable after acute smoke exposure.

Project Dates:
January 1982–December 1983.

Financial Support:
KTHRI.

0907. UNIVERSITY OF KENTUCKY, Departments of Oral Biology and Medicine, Lexington, Kentucky 40536.

Project Title:
Effects of Chronic Cigarette Smoking on Complement and Control Proteins, Immunoglobulins, and Ceruloplasmin.

Principal Investigators:
Bridges, R.B.; Wyatt, R.J.; Rehm, S.R.

Objective:
To determine if chronic cigarette smoking affects the concentration of humoral mediators of inflammation; determine the relationship of the effects to impairment of pulmonary function.

Methods or Approach:
Male smokers (n = 125) and age-matched nonsmokers (n = 125, mean age 35 years) completed questionnaires concerning medical, pulmonary, drug, and smoking histories. Plasma samples were collected and concentrations of 15 complement and control proteins (Clc, C2, C3, C4, C5, C6 C7, C8, C9, Factor B, properdin, Factor H, Factor I, Cl-INH, and C4bp), immunoglobulins (IgA, IgM, and IgG) and ceruloplasmin were determined by radial immunodiffusion. Plasma nicotine and continine concentrations were also determined. Pulmonary function was measured by forced expiratory spirometry and single breath nitrogen test.

Results to Date:
Modest, but significant, elevations in C9, Factor B, Factor I, Cl-INH, and ceruloplasmin were observed in smokers; elevations in C9 and ceruloplasmin were significantly associated with present (cigarettes/day) and cumulative (pack-years) smoking history, and with plasma nicotine and cotinine concentrations. Consistent with relatively young age, smokers had only modest impairment of lung function. Elevations in C9 were significantly associated with impaired function as measured by the single breath nitrogen test, while elevations in

ceruloplasmin were associated with impaired function as measured by both forced expiratory spirometry and the single breath nitrogen test. Of the immunoglobulins measured, only IgG was significantly depressed in smokers; an effect so minimal as to be of questionable biological significance. Results suggest that smoking induces a low-grade inflammatory reaction that results in elevations of "phase reactive" proteins in peripheral blood and that elevations are associated with both smoking history and impaired pulmonary function.

Project Dates:
January 1982–December 1984.

Financial Support:
KTHRI.

0908. UNIVERSITY OF KENTUCKY, Departments of Oral Biology and Medicine, Lexington, Kentucky 40536.

Project Title:
Effects of Chronic Cigarette Smoking on Peripheral Blood Leukocytes and Neutrophil Lysosomal Enzyme Activities.

Principal Investigators:
Bridges, R.B.; Rehm, S.R.

Objective:
To (1) determine effects of chronic cigarette smoking on number and type of peripheral blood leukocytes; (2) study the effect on neutrophil lysosomal enzyme activities; and (3) investigate the relationships between these parameters and pulmonary function as measured by forced expiratory spirometry and the single breath nitrogen test.

Methods or Approach:
Smokers (n = 110) and age-matched nonsmokers (n = 110) were compared according to number and type of peripheral blood leukocytes and lysosomal enzyme activities of isolated neutrophils. Elastase activity was determined using ^{125}I-labeled α-elastin and two synthetic peptide substrates.

Results to Date:
Smokers had a significant elevation (mean, 35 percent) in peripheral blood leukocytes that was attributable to increases in neutrophils (44 percent), lymphocytes (31 percent), and monocytes (23 percent). Elevations in total leukocytes and neutrophils was significantly associated with both present and cumulative cigarette consumption. The number of neutrophils correlated significantly with plasma nicotine and cotinine concentrations; elevations in total leukocytes and neutrophils were associated with impaired pulmonary function (especially as determined by the single breath nitrogen test). Results suggest that leukocytosis associated with smoking is significantly associated with impaired pulmonary function. Smokers were also shown to have a modest elevation in neutrophil myeloperoxidase (MPO) activity/cell, but smoking does not appear to affect neutrophil elastase activity. The activities did not correlate significantly with either smoking history or pulmonary function. Although modest, elevations in neutrophil MPO activity may adversely affect protease-antiprotease balance by catalyzing the oxidative inactivation of α_1-protease inhibitor. Increases in neutrophil number in bronchoalveolar lavage of smokers has been previously observed, which may increase the protease burden of the lung even though elastase activity per cell appears to be unaltered by smoking.

Future Plans:
The mechanism for leukocytosis in smokers and the increase in MPO activity/cell will be investigated.

Project Dates:
January 1982–December 1983.

Financial Support:
KTHRI.

0909. UNIVERSITY OF KENTUCKY, TOBACCO AND HEALTH RESEARCH INSTITUTE, University and Cooper Drives, Lexington, Kentucky 40546.

Project Title:
Reinforcing Properties of Nicotine.

Principal Investigator:
Iwamoto, E.T.

Objective:
To assess why people smoke by examining the relationship between nicotine, reward, and behavior; determine intersubject differences in responses to nicotine in laboratory rats.

Methods or Approach:
It is hypothesized that nicotine dependence arises from nicotine-induced positive reinforcing effects and/or diminution of nicotine-induced aversive effects that are manifested after repeated administration. Intersubject differences in response to nicotine will be investigated. The following models of reward and aversion are being used: (1) subcortical nicotine self-administration; (2) schedule-induced nicotine self-administration; (3) nicotine-induced conditioned place preference and place aversion; (4) nicotine-induced conditioned taste aversion; (5) subcortical nicotine-induced aversion and taste aversion; and (6) nicotine effects on acquisition and retention of autoshaped behavior, spatial alternation, and radial maze performance.

Results to Date:
A dependable subcortical drug delivery system that microinjects nanoliter quantities into discrete brain sites of the rat has been developed. Previous findings have been confirmed that nicotine induces taste aversion in the rat. In addition, data show that preexposure to nicotine obtunds subsequent taste aversion conditioning. It has been demonstrated that nicotine induces both reward and aversion in different subpopulations of rats as assessed by the conditioned place preference paradigm.

Future Plans:
A long-term goal is to develop a laboratory model to detect nicotine-induced reward and nicotine-induced aversion in the rat, to be used to determine if interanimal differences in response to nicotine have a molecular basis.

Project Dates:
August 1981–1987.

0910. UNIVERSITY OF KENTUCKY, COLLEGE OF MEDICINE, Department of Pharmacology, Lexington, Kentucky 40536.

Project Title:
Nicotine Binding Sites in the Rat Brain and the Central Nervous System. Pharmacology of New and Unique Specific Ligands in the Dog.

Principal Investigators:
Martin, W.R.; Sloan, J.S.

Objective:
To (1) resolve the isomers of (±)-2-methylpiperidine, a drug with specificity for the (±)-(^{3}H)nicotine up-regulatory site, and study binding characteristics in the rat whole brain P_2 (synaptosomal) preparation; (2) study binding characteristics of (-)- and (+)-(^{3}H)nicotine to the rat P_2 preparation and the interaction of the (+)- and (-)- isomers with regard to presumed allosteric changes induced by the up-regulatory site; (3) synthesize and study the binding characteristics of (±)-

(^{3}H)-2-methylpiperidine and (^{3}H)acetylcholine; (4) continue to study nicotine congeners and other drugs with the hope of finding drugs that specifically interact with each of nicotine's binding sites; and (5) study the binding characteristics of nicotine in chronically smoked, sham controls and untreated rats to determine if chronic nicotine exposure alters the binding density of nicotine.

Methods or Approach:

The studies use a P_2 preparation of female rat whole brain homogenates. Saturation and competition studies employing a wide variety of nonlabeled compounds are assessed using the filtration technique and (±)-, (-)-, and (+)-(^{3}H)nicotine as the labeled ligands. (±)-(^{3}H)-2-Methylpiperidine and (^{3}H)acetylcholine will be synthesized and binding characteristics assessed. Methylpiperidine (both (-)- and (+)-) has been resolved and ability to compete with binding of (±)-, (-)-, and (+)-(^{3}H)nicotine will be determined. Scatchard data derived from experiments are analyzed by iterative nonlinear, computerized curve-fitting programs that provide a least squares line. Binding characteristics of (-)- and (+)-nicotine and other drugs that exhibit specificity are being compared to using the fourth ventricle of the intact unanesthetized dog. Effects on the EEG, pupils, pulse rate, blood pressure, temperature, and skin twitch reflex latency are studied. Interactions between nicotinic and noncholinergic antagonists (mecamylamine, dihydro-β-erythroidin, and N-benzyl nicotine), (+)- and (-)-nicotine, (±)-2-methylpiperidine, and cytisine are being studied.

Results to Date:

Findings show that nicotine binds to a very high affinity site; an up-regulatory site where it and other drugs can bind and increase the binding density at other sites; a high affinity site and one or two low affinity sites in the P_2 preparation by complex interactions. Using (±)-(^{3}H)nicotine as the labeled ligand, drugs with specificity for the up-regulatory site have been identified; (±)-2-methylpiperidine is the most specific. Of the drugs that do not enhance, or up-regulate, (±)-(^{3}H)nicotine binding, (-)-cytisine appears to have specificity for the high affinity site. Saturation studies using (-)- and (+)-(^{3}H)nicotine revealed that (-)- and (+)-nicotine bind to separate very high and high affinity sites in that the binding density for (-)-nicotine is 10 times greater at these sites than that for (+)-nicotine. The isomers also have different specificities for the up-regulatory sites(s) where (+)-nicotine has both a higher affinity and greater efficacy at both the (-)- and (+)-nicotine sites. Data provide a basis for reconciling the pharmacology of (-)- and (+)-nicotine.

Future Plans:

Binding studies will continue to better characterize the up-regulatory site(s) for nicotine and to develop compounds with even greater specificity as up-regulators and high affinity site agonists. The relevance of binding data to the pharmacology of the drugs is being determined. The effect of a time course of preexposure to key drugs including nicotine, both in vitro and in vivo, on the binding of (^{3}H)nicotine to the P_2 fraction of the rat brain and specific areas of the dog brain will be determined. Drugs with a high degree of specificity for one or more of nicotine's binding sites will be tritiated and binding characteristics studied.

Project Dates:

July 1981–July 1986.

Financial Support:

KTHRI.

0911. UNIVERSITY OF KENTUCKY, Department of Agronomy, Lexington, Kentucky 40546-0091.

Project Title:

Evaluation of Genetic Variability for Low Tar in Burley Tobacco.

Principal Investigators:

Nielsen, M.T.; Collins, G.B.

Objective:

To introduce genetic variability for tar levels into burley tobacco; evaluate new populations for tar delivery by pyrolysis of ground tobacco tissue (particulate matter index, PMI).

Methods or Approach:

Tobacco genotypes previously identified as having low tar delivery will be crossed with a burley tobacco cultivar. Advanced to the F_2 generation, anthers from burley-type plants will be removed and cultured in vitro. An array of 75 to 100 doubled haploid lines from each cross will be generated. Lines will be grown in the field for two seasons; cured tobacco leaves from each line will be ground and analyzed for smoke particulate matter and nicotine delivery.

Results to Date:

Preliminary indications, from first-year field study data, are that a number of doubled haploid lines deliver significantly less tar and nicotine to the smoke than current commercial cultivars of burley tobacco. Several lines had PMIs that were 25 percent or less than the check cultivar.

Future Plans:

Doubled haploid lines possessing low tar delivery will be evaluated for agronomic traits and will be used as breeding lines for genetic improvement of burley tobacco.

Project Dates:

July 1981–June 1985.

Financial Support:

USDA (58-7B30-1-294).

0912. UNIVERSITY OF KENTUCKY, Department of Pharmacology, Research Facility No. 2 MR-117, Lexington, Kentucky 40536.

Project Title:

Changes in Coronary Vascular Reactivity and Arrhythmogenic Threshold Induced by Chronic Exposure to Tobacco Smoke.

Principal Investigator:

Piascik, M.T.

Objective:

To determine whether chronic exposure to tobacco smoke increases coronary vascular reactivity and decreases arrhythmogenic threshold in Sprague-Dawley rats; test whether cadmium in tobacco smoke mediates hyperreactivity.

Methods or Approach:

Animals will be exposed for 5 or 30 weeks to smoke from 2R1 reference cigarettes or cadmium-enriched cigarettes that deliver 10 times the amount of cadmium as 2R1 cigarettes. Animals maintained in cages and sham-smoked animals will serve as control groups. Following exposure, animals will be killed, hearts will be removed and studied. Two parameters to be examined are reactivity of coronary vasculature to the endogenous spasmogen, angiotension II, and threshold for electrically induced ventricular arrhythmias. Cadmium content of the hearts will then be determined.

Results to Date:

To date, only 5-week protocols have been completed; no change in sensitivity of coronary vasculature to angiotensin II following exposure to 2R1 or cadmium-enriched smoke was observed and the threshold for ventricular arrhythmias was not altered. Despite the negative findings, cadmium content of hearts from animals exposed to smoke from cadmium-enriched cigarettes was significantly increased over both control groups and the group exposed to smoke from 2R1 cigarettes, suggesting that cadmium-enriched cigarettes may be a new way to expose animals in cadmium toxicity studies.

Project Dates:
January 1984–December 1984.

Financial Support:
KTHRI (124-05-7H700-5B520).

0913. UNIVERSITY OF KENTUCKY, TOBACCO AND HEALTH RESEARCH INSTITUTE, Cooper and Alumni Drives, Lexington, Kentucky 40546.

Project Title:
Correlation of Pulmonary Function Tests With the Mediators of the Inflammatory Response in the Assessment of Obstructive Airways Disease.

Principal Investigator:
Rehm, S.R.

Objective:
To assess ventilatory indices of obstructive airways disease in cigarette smokers and in nonsmokers matched by age, sex, and race.

Methods or Approach:
Data derived from single breath nitrogen tests and from forced expiratory spirometry are correlated with serum complement and complement-derived chemotactic factors, chemotactic factor inactivators, granulocyte elastase, and serum antielastase activity to test the hypothesis that cigarette smokers vary in susceptibility to development of obstructive airways disease because of variable activity of components of inflammatory response. Forced expiratory spirometry is repeated until three accptable tracings are obtained. The largest forced vital capacity (FVC) and forced expiratory volume in 1 sec (FEV_1) are recorded, even if these do not come from the same curve. For measurement of maximum midexpiratory flow (MMEF) and forced expiratory flow (FEF) 75-85, the "best" curve is chosen (Intermountain Thoracic Society method). The resident gas technique is used to generate single breath nitrogen curves. The slope of phase III is determined from a best fit line between 70 percent and onset of phase IV. Total lung capacity is calculated from the alveolar equation.

Results to Date:
To date, 170 cigarette smokers and 170 matched nonsmokers have been studied. Subjects average 35 years of age, with average smoking history of 18 pack-years, and tend to have small airways dysfunction rather than overt bronchitis and emphysema. Elevations of α_1-protease inhibitor have been found in smokers, and no evidence of oxidative inactivation of the enzyme in peripheral circulation. Smokers with normal pulmonary function do not differ from "normal" smokers in serum markers of smoke exposure, "puff profile," circulating neutrophils, antitrypsin, complement proteins, or micronutrients. However, they do tend to consume alcohol, which may suppress the inflammatory response and minimize development of airflow obstruction.

Project Dates:
January 1981–December 1984.

Financial Support:
KTHRI (5A-518).

0914. UNIVERSITY OF KENTUCKY, COLLEGE OF MEDICINE, Department of Physiology, Lexington, Kentucky 40536.

Project Title:
Effects of Tobacco Smoke Inhalation on Arterial and Capillary Blood Flows in Human Skin.

Principal Investigator:
Richardson, D.

Objective:
To determine effects of acute tobacco smoke inhalation on arterial and capillary blood flow in human skin; determine if effects are graded in accordance to nicotine content of cigarettes.

Methods or Approach:
Twenty female smokers consented to smoke three cigarettes each on separate occasions. Cigarettes (nicotine content, 0.5, 1.0, and 1.9 mg/cigarette, 30 mm butt length) were given to subjects in a random double-blind manner Digital artery (DBV) and nailfold capillary (CBV) blood flow velocities were measured in the second finger of one hand via Doppler ultrasound and video microscopy before and after consumption of a single cigarette. Surface temperature of the finger was maintained at 32° C by circulating warm air over the hand.

Results to Date:
Within 2 minutes of smoking a cigarette, DBV and CBV were significantly decreased ($p \leq 0.05$) compared with values before smoking. However, changes were not related to nicotine content for either variable. To determine relative effects on arterial and capillary blood flow, DBV and CBV data were pooled over all cigarettes. Analysis showed a 48 percent decrease in DBV, but only a 22 percent decrease in CBV. Response difference was significant ($p \leq 0.005$). It is concluded that acute tobacco smoke inhalation has a more pronounced effect on total blood flow than on superficial capillary blood flow in human skin, but neither response is graded to nicotine content of cigarettes.

Project Dates:
October 1982–June 1984.

Financial Support:
KTHRI (5B508).

0915. UNIVERSITY OF KENTUCKY, SCHOOL OF MEDICINE, Department of Microbiology and Immunology, Lexington, Kentucky 40536.

Project Title:
Effect of Cigarette Smoking on the Immune Response.

Principal Investigator:
Sopori, M.

Objective:
To determine effects of exposure to acute and chronic cigarette smoke on immune response in rats, including effects on antibody response to T-independent and T-dependent antigens, antigen presentation, and response of T cells to mitogens.

Methods or Approach:
Three groups of experimental rats were used: bench controls, sham controls (exposed to fresh air), and smoke exposed. In the smoke-exposed group, animals were subjected daily to smoke from reference cigarette 2RI for 4 to 40 weeks. To determine response to T-dependent (TNP-KLH) or T-independent (TNP-BA) antigens, animals were immunized with the antigens 5 days prior to sacrifice and anti-TNP plaque-forming cells (PFC) response for 1 x 10^6 spleen cells was determined by standard protocols.

Results to Date:
Animals exposed to cigarette smoke for more than 25 weeks showed several changes in immune responsiveness, including a significant decrease in PFC response to TNP-KLH, while response to TNP-BA was essentially unaltered. Lymph node T cells from smoke-exposed animals also responded significantly less to concanavalin A, while response to PHA was variable and not significantly different from controls. Significant changes in response of T cells from smoke-exposed animals to alloantigens was not observed. Results suggest that smoking may alter the number or the response of some T cell populations.
Future Plans:
Various T cell subsets are being fractionated to determine cell surface and functional phenotype of lymphocytes that are affected by cigarette smoke.
Project Dates:
July 1984–June 1985. KTHRI (4A023).

0916. UNIVERSITY OF KENTUCKY, Department of Agronomy, N212F Agriculture Science Center North, Lexington, Kentucky 40546.

Project Title:
Studies of the Potential for Reducing Cadmium Accumulation in Tobacco.

Principal Investigator:
Wagner, G.J.
Objective:
To (1) test species and cultivars of tobacco for ability to accumulate cadmium (Cd); (2) determine extent of genetic variability in Cd accumulation potential for *Nicotiana* ; (3) identify species/cultivars that may be use in future breeding programs; and (4) identify Cd forms primarily responsible for accumulation.
Methods or Approach:
Species and cultivars of tobacco were grown in nutrient solution containing 0.5 to 8.0 μg Cd (soil solution levels of Cd in the field). At young seedling stage, plant tops and roots were harvested, frozen, lyophilized, and a portion oxidized and analyzed for Cd to determine Cd/mg dry weight. Relationship of Cd/mg dry weight vs. Cd concentration during growth was established for top and root tissue of each species/cultivar. Another tissue portion was homogenized and fractionated into soluble and insoluble fractions, which were further separated by gel filtration chromatography to determine molecular weights of prominent Cd-binding forms.
Results to Date:
Cultivars of *N. tabacum* vary little in Cd accumulation potential (as measured) in concentration range tested. In contrast, in cultivars of *N. rustica* and *N. rotundifolia*, which accumulated about the same amount of total Cd, most of the metal was concentrated in roots. Accumulation in tissues of all species/cultivars was roughly correlated with amount of an approximately 2,000 dalton Cd-binding species that was present.
Future Plans:
The Cd-binding form will be characterized to substantiate its suspected importance in Cd accumulation. Mature plants will be examined to substantiate results obtained with seedings. Breeding experiments with *N. rustica* and *N. tabacum* will determine if the high root accumulation characteristic can be transferred to cultivated varieties of *N. tabacum*.
Project Dates:
January 1984–December 1984.

Financial Support:
KTHRI.

0917. UNIVERSITY OF KENTUCKY, Department of Physiology and Biophysics, MS-507 Medical Center, Lexington, Kentucky 40536.

Project Title:
Acute Effects of Inhaled Cigarette Smoke on Breathing: The Role of Respiratory Reflexes.

Principal Investigator:
Lee, L.-Y.
Objective:
To elucidate the underlying mechanisms responsible for the acute effects of inhaled cigarette smoke on breathing; assess influence of the effects on development of chronic pulmonary disorders related to smoking.
Methods or Approach:
Ongoing studies are performed in a conscious dog model to avoid suppression of neural reflexes by anesthesia. To determine influence of nicotine contained in cigarette smoke in eliciting acute respiratory effects, and to avoid possible complications caused by a difference in other smoke consitituents, nicotine is added to control cigarettes (low-nicotine research cigarettes) to increase nicotine content in the smoke. Acute respiratory responses to a single puff of cigarette smoke generated by a machine from both control and nicotine-laced cigarettes are determined and compared in the same group of animals.
Results to Date:
It was shown previously that inhalation of cigarette smoke (comparable to a single puff of human smoking) consistently caused acute respiratory responses in awake dogs. Responses consisted of (1) apnea or augmented inspiration triggered immediately after smoke inhalation and (2) delayed hyperpnea. Initial change in breathing pattern was eliminated by cold blocking of both vagi, suggesting that vagal bronchopulmonary sensory afferents were involved. Delayed hyperpnea was due primarily to stimulation of carotid body chemoreceptors, since denervation of the receptors abolished approximately 70 percent of the increase in ventilation. Data suggest that nicotine is the major smoke constituent responsible for elicitation of both the immediate change in breathing pattern and delayed hyperpnea following smoke inhalation.
Future Plans:
Ongoing investigations will (1) identify sites and types of respiratory tract sensory receptors that mediate nicotine-induced respiratory reflexes, and (2) characterize acute respiratory responses to cigarette smoke inhaled through the upper airway.
Project Dates:
July 1984–June 1987.
Financial Support:
KTHRI (4A025).

0918. UNIVERSITY OF KENTUCKY, COLLEGE OF PHARMACY, Lexington, Kentucky 40536.

Project Title:
Cigarette Smoke and Arachidonate Metabolism.

Principal Investigator:
Tai, H.-H.
Objective:
To determine whether arachidonate metabolism in the blood vessel interface and in the lung is disturbed by cigarette smoking, favoring thrombogenesis and atherogenesis; investi-

gate if other hydroperoxy and hydroxy fatty acids are released from pulmonary alveolar macrophages and leukocytes following smoke exposure, recruiting phagocytic cells that release lysosomal proteases and cause damage to alveolar walls.

Methods or Approach:

Recent discovery of the metabolism and actions of arachidonate-derived biologically potent fatty acids appears to provide a plausible biochemical basis of the genesis of thrombosis, atherosclerosis, and emphysema. Thromboxane synthesized by platelets and prostacyclin produced by vascular cells provide a balanced control of vascular homeostasis. Other tissues (such as the lung) that produce both thromboxane and prostacyclin may also contribute to this homeostasis. In addition, products of 12-lipoxygenase pathway released from platelets during aggregation may initiate migration and proliferation of smooth muscle cells leading to development of atherosclerotic plaque. Metabolism of arachidonate in tissues and cells will be studied by using substrate combined with chromatographic techniques. The procedure will be corroborated with radioimmunoassay to determine possible alteration in metabolic profile of arachidonate.

Results to Date:

Sprague-Dawley rats did not show any significant change in either thromboxane or prostacyclin synthesis following up to 16 weeks of cigarette smoke exposure; however, 12-HETE synthetic activity was increased after 16 weeks exposure. Fisher rats also failed to exhibit any change in thromboxane and prostacyclin production after 21 and 36 weeks of smoke exposure. However, catabolism of prostaglandins and thromboxane appeared to show changes as demonstrated by progressive decrease in pulmonary NAD^+-dependent 15-hydroxyprostaglandin dehydrogenase (15-PGDH) activity. Acrolein and oxidizing agents inactivated the enzyme irreversibly, suggesting that smoke components might impair enzyme activity. Because of differential pulmonary catabolism of thromboxane and prostacyclin by lung, decrease in pulmonary 15-PGDH activity may result in increased thromboxane/prostacyclin ratio and consequent disturbance of vascular homeostasis. Although smoking alone did not appear to affect thromboxane and prostacyclin synthesis, smoking plus estradiol treatment significantly increased thromboxane synthetic activity in platelets without affecting prostacyclin production in aorta. Findings may offer a plausible explanation for high incidence of coronary heart disease in women who smoke and take oral contraceptives. Arachidonate was found to metabolize to TXB_2, 5-HETE, and LTB_4 by alveolar macrophages. Smoking appeared to decrease enzyme activities leading to 5-HETE and LBT_4 synthesis, presumably due to prior activation of macrophages by smoke particles or components. Levels of TXB_2 in bronchial lavage fluid were significantly increased in most cases and levels of LTB_4 were also elevated in one instance after smoke exposure.

Future Plans:

Future studies will (1) explore other possible mechanisms of decrease in 15-PGDH activity; (2) examine whether such a decrease is reversible; (3) investigate arachidonate metabolism in lung, particularly the lipoxygenase pathway; (4) identify metabolites of arachidonate in rat neutrophils; and (5) determine effect of cigarette smoke on arachidonate metabolism in neutrophils.

Project Dates:

January 1984–December 1986.

Financial Support:

KTRB (5B-521).

0919. UNIVERSITY OF KENTUCKY, COLLEGE OF PHARMACY, Lexington, Kentucky 40536.

Project Title:

The Role of Lipoxygenase Pathway in the Development of Emphysema.

Principal Investigator:

Tai, H.-H.

Objective:

To (1) provide evidence for a role of 5-lipoxygenase pathway in releasing elastase and myeloperoxidase induced by cigarette smoke; (2) examine if cigarette smoking stimulates biosynthesis of lipoxygenase products and platelet activating factor in platelets and neutrophils; and (3) investigate whether stimulation of the lipoxygenase pathway and biosynthesis of platelet activating factor (PAF) by smoking contributes significantly to the underlying mechanisms of increased release of proteases and oxidative species commonly found in smokers.

Methods or Approach:

Pathogenesis of chronic obstructive pulmonary disease is thought to be due to an imbalance between elastase and α_1-antitrypsin (elastase from neutrophils, α_1-antitrypsin from the liver into plasma). It is postulated that cigarette smoke may first stimulate lung phagocytic cells to release chemotactic factors and PAF, which cause neutrophils to accumulate in the lung and to release elastase, myeloperoxidase, and other oxidative species, which may lead to predominant influences of elastase in lung and may result in destruction of alveolar walls. Arachidonate lipoxygenase products from neutrophils, alveolar lung macrophages, and platelets are potent chemotactic, chemokinetic, and degranulating agents. PAF from the same cells is also a potent chemotactic and degranulating agent and may work in concert with lipoxygenase products to potentiate action. Biosynthesis of lipoxygenase products will be studied using labeled arachidonate combined with chromatographic techniques, corroborated with radioimmunoassay. Studies on biosynthesis of platelet activating factor will be aided by bioassay procedure and cell prelabeling technique using labeled lyso platelet activating factor as a precursor.

Results to Date:

The major metabolites of arachidonate in human neutrophils are LBT_4, 5-HETE, and 15-HETE. Human neutrophils can be stimulated in a dose-dependent manner to release elastase and myeloperoxidase and LTB_4 by PAF, chemotactic peptide FMLP, and calcium ionophore A-23187. Maximal stimulation occurs at 1 μm of each agonist. Release of elastase and myeloperoxidase can be blocked by lipoxygenase inhibitors, but not by cyclooxygenase inhibitor, suggesting lipoxygenase metabolites may mediate enzyme release. LTB_4 was found to be a potent inducer of elastase and myeloperoxidase release, and to provide more direct evidence that LTB_4 may mediate enzyme release caused by PAF or chemotactic peptide, a sensitive and specific radioimmunoassay for LTB_4 was developed. PAF, FMLP, and A-23187 were able to stimulate LTB_4 synthesis in addition to elastase and myeloperoxidase release. Lipoxygenase inhibitors blocked both LTB_4 synthesis and enzyme release induced by the agonists. However, LTB_4 appeared to be a necessary, but not sufficient, agent to mediate enzyme release. Both protein kinase C activation and calcium mobilization are required for maximal enzyme release. The calcium channel blocker verapamil inhibited enzyme release induced by PAF or FMLP. Findings support the hypothesis that PAF and chemotactic factor induce elastase and myeloperoxidase release from neutrophils and that arachidonate metabolites, particularly LTB_4, play a necessary role in mediating enzyme release.

Future Plans:
Studies will (1) examine whether PAF or FMLP induced synthesis of LTB$_4$ from endogenous store of arachidonate is altered by cigarette smoking; (2) examine effect of cigarette smoking on PAF biosynthesis in phagocytic cells; and (3) investigate arachidonate metabolism and release of elastase and myeloperoxidase from human alveolar macrophages induced by smoke condensate, zymosan, and chemotactic factors.
Project Dates:
January 1984–December 1985.
Financial Support:
KTRB (5A-525).

0920. UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Interaction of Nitrogen and Chloride Fertilizer on Health Related Constituents of Burley Tobacco.

Principal Investigators:
Sims, J.L.; Davis, D.L.
Objective:
To determine effects of the interaction of form of nitrogen (N) and chloride (Cl) fertilizer on concentrations of organic acids mineral cations and anions, total volatile acids, total volatile bases, tar, and other chemicals and physical traits; determine effect of form of nitrogen and chloride fertilizers on selected chemical parameters of cigarette smoke.
Methods or Approach:
Laboratory, greenhouse, and field experiments utilizing burley tobacco will be conducted to determine how the form of chloride and nitrogen affects dry matter in plants. Different ratios of ammonium/nitrate, nitrogen, and two sources of potassium will be tested. Agronomic and chemical information will be obtained.
Results to Date:
Field experiments were conducted at Lexington, Kentucky, during 1981 and 1982. Burley tobacco plants treated with ammonium (NH_4) fertilizer had higher dry weights early in the growing season than plants receiving nitrate (NO_3) fertilization. Highest cured leaf yields were obtained from treatments containing either 75 percent NO_3:25percent NH_4 or 100 percent NO_3 fertilizer. Plants treated with potassium chloride (KC1) fertilizer produced lowest dry weights early in the season but highest cured leaf yields when compared with potassium sulfate (K_2SO_4). Greater amounts of C1 were absorbed in the presence of NH_4 than NO_3, and concentrations of plant NO_3 and C1 were inversely related. This relationship occurred for both the 35-day samples and cured leaf tissue. The effect of form of N was greater in the presence of KC1 than K_2SO_4. Concentrations of nitrogenous constituents in leaf were highest in the presence of NO_3 and K_2SO_4 fertilizers. Burn rates of cured leaf were much higher for K_2SO_4 than KC1 treated tobaccos. Within KC1 treatments rates increased slightly as level of NO_3 fertilizer increased. Concentrations of C1 in cured leaf were highest in the flyings leaf group, and spring application of KC1 gave a concentration about half that of fall application.
Project Dates:
June 1981–June 1983.
Financial Support:
USDA (7012-20881-020S).
References:
(1) Eivazi, F.; Sims, J.L.; Casey, M., et al. "Growth and Molybdenum Concentration of Burley Tobacco as Influenced by Potassium, Molybdenum, and Chloride in Transplant Fertilizer Solutions." *Canadian Journal of Plant Sciences* 63(2):531-538, April 1983. (2) Eivazi, F.; Sims, J.L.; Leggett, J.E. *Phosphorus and Molybdenum Interaction Effects on Concentration of Molybdenum by Burley Tobacco Plants.* 95th Annual Report of Kentucky Experimental Station, 1983.

0921. UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Carbon-Nitrogen Ratio in Tobacco and Relationship to Health Related Constitutents.

Principal Investigators:
Leggett, E.; Simms, J.L.; Hamilton, J.L.
Objective:
To (1) determine soluble and insoluble pools of carbon (C) and nitrogen (N) and their interrelationship with N fertilizer and carbon dioxide (CO_2); (2) study influences of plant C and N content on green leaf particulate matter index (PMI); (3) evaluate influence of plant C and N fractions on quality of carbohydrates and N fractions; and (4) determine influence of the C and N content on smoke chemistry.
Methods or Approach:
Greenhouse gravel culture and field experiments will be conducted to determine effects of N-sources (nitrate vs. ammonium) on the carbohydrates and the C/N value; pool size of structural and nonstructural carbohydrates and soluble and insoluble N components of leaf; and effect of C/N value on PMI, nicotine, and N-nitrosonornicotine. Chemical analysis of samples will include total nitrogen, total amino acids, protein, total carbohydrates, sugars, inorganic acids, cations and N-nitrosonornicotine.
Results to Date:
Flue-cured and burley experiments were conducted as planned in 1982. Both crops were cured, weighed, and sampled. Green samples were stored in a low temperature freezer and will be freeze-dried. The 1981 samples are being analyzed. Cigarettes were made and assayed for total particulate matter, nicotine, and tar for the flue-cured crop, and the burley crop is being assayed. Although data is incomplete, yield acre value, price per pound, acre index value, and index value for the 1982 flue-cured crop were lower than for the 1981 crop, reflecting excess water damage. Differences among N sources in agronomic features are not great in the 1982 flue-cured crop; neither were there large differences among N sources for smoke characteristics in the 1981 flue-cured crop.
Project Dates:
July 1980–June 1984. ΣDA (7009-20881-017S).

0922. UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Contribution of Cell Wall and Soluble Cell Fractions to Particulate Matter in Tobacco.

Principal Investigators:
Bush, L.P.; Hamilton, J.L.
Objective:
To determine contribution of cell wall and soluble cell fractions to particulate matter index (PMI) of burley and flue-cured tobacco.
Methods or Approach:
The contribution of surface waxes, ethanol extractables, nicotine, cellulose, and their interaction and cell content fractions obtained by serial extraction to particulate matter in burley and flue-cured tobacco will be measured. Components

(altered in accelerated curing with oxygen) that lower particulate matter will be determined. Selected commercially available cultivars and tobacco introductions will be analyzed for cell content and cell wall contribution to particulate matter. Effects of cultural management techniques on particulate matter in burley tobacco will be assessed.

Results to Date:
Samples for total particulate matter (TPM) and ethanol residue, cell wall, and cellulose plus lignin analysis were 200 or 400 lb N/acre burley 21 and low alkaloid (LA) burley 21 tobacco. Nitrogen had little effect on TPM or cellular analysis. LA burley 21 had higher amounts of ethanol residue, cell wall, and cellulose plus lignin and lower ethanol solubles, TPM, and nicotine than burley 21. Capillary gas chromatographic analysis with flame ionization detector was completed on the solvent solubles. Only the hexane, cyclohexane, and chloroform samples contained sufficient volatiles for analysis. In hexane and cyclohexane, the fraction with retention time of about 51 min was the major peak. On the basis of solubilities and analysis, this should be neophytadiene. The second largest peak in hexane and cyclohexane and largest peak in chloroform had a retention time of 48 to 49 min and probably was nicotine. In the hexane solubles, nicotine was 10.12 percent of the volatiles eluted and neophytadiene was 80.92 percent. A fraction eluting at 58.99 min accounted for 1.14 percent of the volatiles, and no other fractions reached 1 percent of the total. In the cyclohexane solubles, nicotine and neophytadiene were 41.9 and 43.8 percent of the volatiles, and no other fractions reached 1 percent of the total. In the cyclohexane solubles, nicotine and neophytadiene were 41.9 and 43.8 percent of total volatiles. The fraction at 59 min was 3.3 percent of the total, and fractions eluting at 62.1 and 69.8 min were just over 1 percent of the total cyclohexane-soluble volatiles. In the chloroform fraction, nicotine was 83.2 percent and neophytadiene 10.8 percent of total volatiles.

Project Dates:
July 1980–September 1982. ΣDA (7006-20881-014S).

0923. UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Chemical Characterization of Tobacco Quality.

Principal Investigator:
Davis, D.L.

Objective:
To (1) characterize the semivolatile oils from burley and dark tobacco; (2) elucidate biosynthetic aspect of tobacco terpenoids; (3) determine the influence of curing on the semivolatile oils; and (4) elucidate the mechanism of cadmium (Cd) accumulation in tobacco, with the long-range goal of manipulating this mechanism so as to reduce Cd accumulation.

Methods or Approach:
The semivolatile oils from commercial cultivars of burley, dark fire-cured, and dark air-cured tobacco types produced under conventional cultural practices will be extracted, fractionated, and characterized by infrared, ultraviolet-vis, nuclear magnetic resonance and capillary gas-liquid chromatography/mass spectrometry analyses. The biosynthesis of terpenoids and major flavor and aroma constituents will be studied. Genotypes that differ in some of the precursor components such as carotenoids and diterpenes will be examined using the above techniques and ^{14}C metabolite experiments. Many of the terpenoids and other semivolatile constituents may be altered during growth and curing phases; therefore, detailed evaluation of these factors in influencing leaf chemistry will be conducted using cultivars of each tobacco type and curing under the appropriate regime.

Results to Date:
Several tobacco varieties that have accessible germplasm have been surveyed, and what appears to be genetic variability in Cd accumulation potential has been identified. Preliminary results show that the amount of a Cd-binding protein occurring in a given variety may vary with the accumulation potential of that variety. Methods for efficiently monitoring this protein and studying its character are being developed. In addition to the research on Cd accumulation, an attempt is being made to develop more efficient methods for introducing radiolabeled precursors of leaf-trichome-exudate terpenoids of tobacco. A method has been devised that results in the conversion of about 1 percent of introduced ^{14}C-acetate into exudate constituents, and the products of labeling are being identified.

Project Dates:
July 1980–June 1985.

Financial Support:
USDA.

0924. UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Effect of Tobacco Type and Curing Method on Terpenoid Fractions.

Principal Investigators:
Davis, D.L.; Chortyk, O.T.

Objective:
To identify, characterize, and quantitate terpenoid compounds of tobacco.

Methods or Approach:
Terpenoid compounds will be isolated and identified by use of gas chromatography (GC), nuclear magnetic resonance, and infrared, ultraviolet, and mass spectrometry (MS). A "fingerprint" procedure will be developed and terpenoids will be separated into classes. Distributions of terpenoids will be examined in the following tobacco samples: air-cured burley and flue-cured tobacco; homogenized leaf cured (HLC) tobacco from the two types using modified HLC techniques; HLC material produced from high-density field plant population; "aged" HLC material; freeze-dried tobacco; and modular cured, flue-cured type and bulk-cured burley tobacco.

Results to Date:
Laminae of burley tobacco cultivar Kentucky 14 were analyzed from the fifth week after transplanting through air-curing for changes in the levels of neophytadiene, a flavor- and aroma-enhancing component, and in saturated aliphatic hydrocarbons and free solanesol. Neophytadiene levels increased during growth, with the most rapid increase occurring after harvesting; final levels of more than 0.1 percent of dry lamina throughout growth and curing, but variations in the relative abundance of individual isomers, were observed. Free solanesol increased throughout growth and curing to a concentration of 4.5 percent of the dry lamina weight when fully cured, and its increase could not be attributed to release from a static pool of solanesol esters. Over 150 constituents were characterized in a steam distillate of 100 kg of air-cured burley tobacco. The extract was fractionated by column chromatography and preparative GC prior to GC/MS. Identified compounds included acids, aldehydes, ketones, esters, ethers, hydrocarbons, lactones, and phenols. Several of the steam-volatile compounds are related to the quality of the tobacco. Several of the terpenoids (e.g., α- and β-Ionone, β-damascenone, β-cyclocitral) were subjected to quartz tube pyrolysis, and

polynuclear aromatic hydrocarbons were determined. At 800° C, α- and β-ionone yielded styrenes, indenes, naphthalene, ionene, and alkylnaphthalenes as major products.

Project Dates:
June 1979–June 1983.

Financial Support:
USDA (7002-20880-001-1).

0925. UNIVERSITY OF KENTUCKY, Department of Agricultural Engineering, Lexington, Kentucky 40506.

Project Title:
Moisture Diffusion and Chemical Composition Changes During Curing of Burley Tobacco.

Principal Investigators:
Walton, L.R.; Henson, W.H.; Burton, H.R.

Objective:
To (1) develop a mathematical model of moisture diffusion from curing burley leaf, based on cellular structure; (2) determine the effect of plant density and airflow rate on drying rate; (3) determine the effect of air temperature and vapor pressure gradient on selected chemical constituents associated with consumer acceptance and health hazards and their leaf precursors; and (4) determine the relationship between temperature-drying rate and these selected chemical constituents.

Methods or Approach:
A mathematical model of moisture diffusion during curing will be developed by solving the vapor diffusion equation subject to cell geometry and appropriate boundary conditions (including epidermal resistance). The effect of plant density and airflow on drying rate will be determined experimentally using three plant densities and three airflow rates. The drying rate of the plant components (lamina, midrib, and stalk) will be determined by sampling. To determine the effect of temperature on chemical changes during curing, tobacco will be cured at three levels of temperature with a constant vapor pressure gradient. To determine the effect of drying rate on chemical changes, tobacco will be cured with a constant temperature at three different vapor pressures.

Results to Date:
Project is in a preliminary phase.

Project Dates:
January 1984–December 1983.

Financial Support:
USDA (KY00146).

0926. UNIVERSITY OF KENTUCKY, Department of Agronomy, Lexington, Kentucky 40506.

Project Title:
Influence of Cultural Management Systems on Nicotine Content in Burley Tobacco.

Principal Investigators:
Atkinson, W.O.; Sims, J.L.; Calvert, J.

Objective:
To develop cultural management systems for increasing accumulation of nicotine in cured leaves of burley tobacco; compare effects of nicotine-influencing regimes on yield, value, and usefulness of burley tobacco to cigarette manufacturers.

Methods or Approach:
Burley tobacco will be grown in replicated field plots with different rates and application times of nitrogen (N) fertilizer, with different soil water regimes and varied plant populations and topping times. Nicotine analyses of green leaf samples taken at different times during the growing season and of cured leaves will be made to determine effects of cultural practices on nicotine accumulation. Quality assessments of cured leaves will be made to ensure that usefulness of tobacco produced under the above conditions will not be impaired.

Results to Date:
Burley tobacco was grown in field plots with nitrogen fertilizer rates of 224 and 448 kg/ha of nitrogen applied either prior to transplanting or in two applications after transplanting. Also, populations of 7,300, 9,000, and 11,700 plants/ha were field-produced and each population topped prior to flowering and 10 days later when 50 percent of the plants had open flowers. A third phase measured the effect of application of several growth regulators on nicotine and particulate matter index (PMI) at 45 or 32 days prior to harvesting. Results showed that (1) 448 kg/N/ha increased nicotine content of cured burley tobacco by an average of 18 percent, but time of application had no effect; (2) varying plant population had no effect, but early topping increased nicotine content by 19 percent; and (3) application of growth regulators caused a variation in nicotine content of 2.65 to 4.15 percent, with untreated tobacco averaging 3.66 percent. PMI values of growth regulator treated tobacco ranged from 52.5 to 71 when the value for untreated tobacco was 59. PMI content was considered an indication of tar content of pyrolized tobacco.

Project Dates:
July 1977–September 1982.

Financial Support:
USDA (KY00153).

0927. UNIVERSITY OF KENTUCKY, Department of Agronomy, Lexington, Kentucky 40506.

Project Title:
Action of Dinitroaniline Herbicides in Soil and Plant Tissues.

Principal Investigators:
Lin, P.P.; Phillips, R.E.; Rieck, C.E.

Objective:
To (1) determine the interrelationship of adsorbed, vapor, and solution phases of dinitroaniline herbicides in soil as affected by soil water, organic matter, and temperature; (2) determine phytotoxicity of vapor and solution of dinitroanilines to plant roots; (3) determine adsorption of dinitroaniline herbicides by plant roots and its subsequent effects upon membrane properties and ion.

Methods or Approach:
Amounts of ^{14}C-labeled dinitroanilines adsorbed onto the soil and dissolved in the soil water will be determined by centrifugation, liquid scintillation spectrophotometry, and gas chromatography. The vapor of the herbicide will be trapped and quantitated by a special gas flow system, including a Florisil column. Vapor phytotoxicity to crop plants of interest will be studied in a specially designed system that prevents direct contact between plant roots and herbicide-treated soil and/or solution. 8.Rb will be used to study effects of dinitroanilines on membrane properties (ion transport) of plant root tissue.

Results to Date:
Primary sites of action of dinitroaniline herbicides are apparently located either on the surface of plant root tissue (plasma membrane) or in root tissue cells. The herbicides have been shown to cause inhibition of cell division resulting from destruction of mitotic activity of cells in the meristem region of root tissue. To examine the relation of herbicides (e.g. dinitramine and trifluoralin) to mitotic activity of root cells, experiments were carried out to determine effects of herbicides on polyamine metabolism in the tissue. Enzymes involved in putrescine formation and polyamine contents in root tissues of

germinating soybean, tobacco, corn, pea, and barley have been characterized. Effects of treatment of the herbicides on enzyme activities and polyamine titers are currently under investigation.

Project Dates:
July 1979–June 1984.

Financial Support:
USDA (KY00225).

Reference:
Lin, P.P.-C. "Polyamine Metabolism and its Relation to Response of the Aleuroe Layers of Barley Seeds to Gibberellic Acid." *Plant Physiology* (In press), 1984.

0928. UNIVERSITY OF KENTUCKY, Department of Agricultural Engineering, Lexington, Kentucky 40506.

Project Title:
Carbon Monoxide Reduction in Cigarette Smoke From a Tobacco Matrix.

Principal Investigators:
Yoder, E.E.; Bunn, J.M.

Objective:
To reduce the yields of carbon monoxide and other undesirable smoke components through modification of physical structure of leaf tobacco in cigarettes.

Methods or Approach:
Using homogenized leaf curing (HLC) materials and other selected tobacco materials, a matrix of continuous longitudinal conduits was formed. The geometric structure of the tobacco matrix was constructed to induce uniform and better combustion of a cigarette. The matrix web thickness and the radial gradient of void ratio for the matrix cross-section were specifically selected for optimum uniformity of mainstream flow and for reduced combustion temperatures. Experimental cigarettes will be smoked under standard conditions and the delivery of CO, NO_x, and other major smoke constituents will be determined in comparison with controls made of conventional materials.

Results to Date:
A problem in developing a laboratory procedure for constructing the experimental cigarette by deforming reconstituted sheet in 60 degree-vee plate dies has been the separation of the sheet at the apex of the die grooves, caused by stretching the tobacco during simultaneous engagement of the sheet through the entire length of the plate. This problem is particularly critical when crimping sheets in dies having a pitch exceeding 0.040 inches. Many variables were examined (including steam treatment of the tobacco) to increase its deformation tolerance. Also, various flexible films, such as teflon and rubber between the tobacco sheet and the dies (0.0575 inches and 0.06250 inches pitch), were tried. Although these treatments reduced the tearing of the tobacco sheet, the separation of the sheet at the apex was so extensive that bonding of the crimped sheet to the flat sheet was not practical. The procedure of spirally wrapping a composite section, formed by a vee-crimped sheet bonded to a flat sheet appears to have the greatest potential for controlling the air flow through the experimental cigarette.

Project Dates:
June 1978–February 1983.

Financial Support:
USDA (1090-20833-009S).

0929. UNIVERSITY OF KENTUCKY, Department of Agronomy, Lexington, Kentucky 40506.

Project Title:
Degradation of Tobacco Carotenoids.

Principal Investigators:
Burton, H.R.; Kasperbauer, M.J.

Objective:
To determine the influence of oxygen, ultraviolet light, and singlet oxygen photosensitizer on degradation of tobacco carotenes; identify degradation products.

Methods or Approach:
The major carotenoids of tobacco (carotene, lutein, violaxanthin, and neoxanthin) will be isolated from burley tobacco. (Carotenoids may be possible precursors of smoke polynuclear aromatic hydrocarbons and/or smoke flavor components.) The purified carotenoids will be exposed individually to ultraviolet radiation and oxygen in the presence and absence of a photosensitizer. The optimum wavelength for degradation will be investigated. The reaction mixtures will be steam distilled to isolate volatile components, which are believed to be tobacco flavor compounds. Isolates will be fractionated and analyzed by glass capillary gas chromatography (GC-2) and GC-2/mass spectrometry. When possible, major components will be synthesized for unambiguous identification. High pressure liquid chromatographic methods will be developed to analyze nonvolatile degradation products. Major degradation products will be subjected to photosynthesis under the same conditions as the original carotenoids.

Results to Date:
Results are not yet available.

Project Dates:
July 1983–June 1985.

Financial Support:
USDA (7008-20880-004S).

0930. UNIVERSITY OF KENTUCKY, Department of Plant Pathology, Lexington, Kentucky 40506.

Project Title:
Influence of Blue Mold on Health Related Constituents of Tobacco.

Principal Investigator:
Kuc, J.

Objective:
To determine the effects of blue mold disease of burley and flue-cured tobaccos on health-related chemical constituents (selected terpenoids and phenolics); determine mechanisms of resistance to tobacco blue mold disease.

Methods or Approach:
Low levels of blue mold inoculum will be introduced into leaves, stems, and roots of tobacco plants. Plants will be subsequently inoculated with high levels of inoculum. Development of disease will be studied in this and unprotected (no low-level inoculation) plants. Protected plants will be analyzed for protective types of biochemicals, which will be bioassayed using blue mold inoculum. The plant metabolism responding to produce such protective biochemicals will be studied.

Results to Date:
Recognition by a plant of the pathogen as "nonself" and a subsequent response are important aspects of resistance. Effectiveness of the response is determined partly by the speed and magnitude with which host-genetic information is expressed. A new technique for systemically immunizing tobacco against blue mold was developed that utilizes restricted infection by the pathogen, *Peronospora tabacina* , to activate

resistance mechanisms. Immunized plants were 95 percent protected against blue mold. There was no necrosis or sporulation. Immunized, unchallenged plants at the start of flowering were 40 percent taller and 30 percent heavier in fresh weight (50 percent in dry weight), had five to seven more leaves, and flowered 2 to 3 weeks before controls. To study the movement of a systemic protection factor, plant stems were girdled either 10 cm above or below the induction site at 3-day intervals up to 21 days after induction. Plants girdled above the site of induction at day 6 or earlier remained susceptible to blue mold, though enhanced growth was evident with the 6-day girdling. Systemic resistance and enhanced growth were evident in plants girdled below the site of induction and when girdling occurred above the site of induction at day 9 or later.

Project Dates:
July 1980–June 1983.

Financial Support:
USDA (7005-20881-001S).

References:
(1) Guedes, M.E.; Kuc, J.; Hammerschmidt, R., et al. "Accumulation of Six Sesquiterpenoid Phytoalexins in Tobacco Leaves Infiltrated With *Pseudomonas lachrymans*." *Phytochemistry* 21:2987-2988, 1982. (2) Kuc, J. "Induced Immunity to Plant Disease." *Bioscience* 32:854-860, 1982. (3) Tuzun, S.; Kuc, J. "A New Technique Which Immunizes Against Blue Mold (*Peronospora tabacina*) and Increases Growth of Tobacco." *Phytopathology* 1982.

0931. UNIVERSITY OF KENTUCKY, Department of Plant Pathology, Lexington, Kentucky 40506.

Project Title:
Modification of Gene Expression in Tobacco by Viral RNA.

Principal Investigator:
Shaw, J.G.

Objective:
To determine effects of virus infections of burley tobacco on health-related chemical constituents (selected alkaloids and terpenoids) in the leaf; determine interaction mechanisms of virus particles and tobacco protoplasts during initiation of infection.

Methods or Approach:
Leaves of susceptible burley tobacco varieties will be mechanically inoculated with purified virus preparations and incubated under controlled conditions. Leaves from infected and control plants will be harvested and chemical analyses made in the University of Kentucky Leaf Analysis Laboratory. Tobacco leaf protoplasts will be inoculated with labeled tobacco mosaic virus and at intervals will be fractionated to determine the radioactivity passing from the virus to subcellular organelles; this will be related to changes in virus particle structure during initiation of infection.

Results to Date:
Project is in a preliminary phase.

Project Dates:
June 1983–June 1985.

Financial Support:
USDA (7023-20881-032S).

0932. UNIVERSITY OF KENTUCKY, APPALACHIAN FRUIT RESEARCH LABORATORY, Lexington, Kentucky 40506.

Project Title:
Design and Manufacture of Low-Yield Reference Cigarettes for Tobacco Safety Research.

Principal Investigators:
Davis, L.D.; Tso, T.C.

Objective:
To design, manufacture, and analyze low-yield reference (LYR) cigarettes for tobacco safety research.

Methods or Approach:
Criteria will be established by an expert panel. Specific characteristics of the LYR will be determined. LYR will be manufactured, inspected, tested, and accepted.

Results to Date:
Specifications developed by a panel of experts were aimed at a target delivery of 11 mg (FTC) tar and 0.7-0.9 mg nicotine/cigarette. The cigarette was designated as 1R4F in accordance with the system used by the Tobacco and Health Research Institute. Approximately 23.2 million cigarettes were manufactured using a standard tobacco blend. Those for the USDA-NCI inventory were packaged in white packs and those for the University of Kentucky in blue packs as specified in the original contract. Results of analyses by six independent laboratories revealed a length of 83.76 mm, a circumference of 24.94 mm, a dilution of 28.4 percent, and a butt length mark of 35 mm. The filler contained 2.10 percent total alkaloids, 9.4 percent reducing sugars, and 2.7 percent glycerine. The cigarette delivered 9.2 mg FTC tar, 0.80 mg nicotine, 11.6 mg carbon monoxide, and 0.34 mg nitrogen oxide, with a puff count of 9.2 when smoked to a 35 mm butt length under standard smoking conditions. Additional physical properties include weight (1.072 gms), RTD (5.4), burn rate (552 sec/40 mm), and pack moisture (12.93 percent). This low-yield cigarette will contribute to future research on smoking and health problems because it represents an increasing percentage of the domestic cigarette market.

Project Dates:
June 1982–November 1983.

Financial Support:
USDA (1090-20882-011S).

0933. UNIVERSITY OF KENTUCKY, Department of Plant Pathology, Lexington, Kentucky 40506.

Project Title:
Influence of Virus Infection on Health-Related Terpenoids and Other Chemical Constituents of Tobacco.

Principal Investigators:
Shaw, J.G.; Davis, D.L.

Objective:
To determine the effects of virus infections of burley and flue-cured tobacco on health-related chemical constituents (selected alkaloids and terpenoids) in the leaf; determine interaction mechanisms of virus particles and tobacco protoplasts during initiation of infection.

Methods or Approach:
Leaves of susceptible burley and flue-cured tobacco varieties will be mechanically inoculated with purified virus preparations and incubated under controlled conditions. Leaves from infected and control plants will be harvested and chemical analyses made in the University of Kentucky Leaf Analysis Laboratory. Tobacco leaf protoplasts will be inoculated with labeled tobacco mosaic virus and at intervals will be fractionated to determine the radioactivity passing from the virus to subcellular organelles; this will be related to changes in virus particle structure during the initiation of infection.

Results to Date:
A single tobacco variety, Ky 16, and two viruses, tobacco etch virus (TEV) and tobacco vein mottling virus (TVMV), were selected for a more detailed study of the concentration of

terpenoids in healthy and infected tobacco leaves. Infection of KY 16 with either of these viruses resulted in substantial reductions in several (as yet unidentified) compounds in the volatile fraction. The genomic RNA TVMV was translated in a cell-free system derived from rabbit reticulocytes. Antisera against TVMV coat protein, TVMV cyclindrical inclusions, the helper component required for aphid transmission of TVMV, and the 49 kd nuclear inclusion proteins of TEV were used to characterize the translational products. Each of the five antisera precipitated a distinctive pattern of polypeptides. Specificity of immunoprecipitation was shown by competing with the various proteins to which antisera were raised and by sequentially precipitating with two different antibodies. These experiments showed that the five antisera define five different nonoverlapping regions of the TVMV genome.

Project Dates:
June 1981–June 1983.

Financial Support:
USDA (7011-20881-019S).

0934. UNIVERSITY OF KENTUCKY, BELKNAP CAMPUS, SCHOOL OF MEDICINE, Exercise Physiology Laboratory, Louisville, Kentucky 40292.

Project Title:
Cigarette Smoking, Physical Activity, and Alcohol Consumption: Relationship to Blood Lipids and Lipoproteins in Premenopausal Females.

Principal Investigators:
Stamford, B.A.; Matter, S.; Fell, R.D., et al.

Objective:
To determine relationships between blood lipid and lipoprotein levels (as dependent variables) and cigarette smoking, physical activity, and alcohol consumption from partial regression coefficients.

Methods or Approach:
Subjects (164 premenopausal females) were randomly selected for evaluation from a much larger pool of volunteers. Initial screening was conducted by questionnaire. Laboratory analyses included treadmill stress testing, body fat assessment, and blood lipid and lipoprotein determinations. Subjects completed questionnaires concerning smoking status and medication and were interviewed concerning physical activity patterns. Most of the 56 smokers averaged 32 cigarettes/day. Blood samples were obtained following 12 hours of fasting and abstinence from smoking. Two fitness categories were assigned: low category for those who performed little or no regular exercise, and high category for regular joggers or runners.

Results to Date:
A lower HDL-C level (10.1 mg/dL) was seen in smokers than in nonsmokers. For each ounce of alcohol consumed, HDL-C level was higher by 2.8 mg/dL, and greater physical activity was associated with a higher HDL-C level of 8.6 mg/dL. An analysis of covariance with covariance adjustments for age and body fat revealed that smokers who regularly exercise or consume alcohol had significantly lower HDL-C levels than nonsmokers with similar habits. Subjects who exercise and consume alcohol demonstrated higher HDL-C levels than those who indulge in one or the other separately. Results suggest that cigarette smoking may attenuate effects of chronic exercise or alcohol consumption, or of both, to raise HDL-C levels. Also, chronic exercise and alcohol consumption may exert an additive effect, raising HDL-C level.

Financial Support:
AHA; University of Kentucky.

Reference:
Stamford, B.A.; Matter, S.; Fell, R.D., et al. "Cigarette Smoking, Physical Activity, and Alcohol Consumption: Relationship to Blood Lipids and Lipoproteins in Premenopausal Females." *Metabolism* 33(7):585-590, July 1984.

0935. UNIVERSITY OF LOUISVILLE, SCHOOL OF MEDICINE, Department of Pharmacology and Toxicology, Louisville, Kentucky 40292.

Project Title:
Inhibition of Localization of Sidestream Smoke Carcinogens in Epithelial Tissues.

Principal Investigator:
Waddell, W.J

Objective:
To determine which compounds block the accumulation of specific smoke carcinogens in bronchial epithelium and other epithelial tissues where these carcinogens accumulate.

Methods or Approach:
Commercially available N'-nitrosonornicotine-^{14}C will be injected intravenously into male and female C57Bl/6J mice. The mice will be sacrificed by freezing in dry ice/hexane at -70°C. These frozen mice are embedded in carboxylmethylcellulose and then sectioned at -20°C to obtain 20μ-thick whole-body sagital sections onto Scotch tape. The animals are sectioned so that all the tissues in the body are sampled. The sections are allowed to freeze-dry; once dry these sections are firmly attached to x-ray film and allowed to expose in the dark at -20°C. The sections, still attached to the Scotch tape, are separated from the x-ray film, and the film is developed and fixed. Areas of blackening on the film indicate accumulation of radioactivity. This whole-body autoradiographic procedure for water-soluble compounds does not allow thawing or any translocation of radioactive material. Thus the distribution seen on the autoradiograph represents the in vivo disposition of the compound and/or its metabolites at the time of sacrifice. This is a continuation of an earlier project that revealed a remarkable correlation of localization of metabolites of nitrosonornicotine (NNN) in the sites of tumor formation. Since this is the first carcinogen in tobacco smoke to show this correlation, the procedure of whole-body autoradiography offers many possibilities for study. For example, compounds which block the localization of the metabolites of NNN in bronchial epithelium should prevent the carcinogenic action. This block of accumulation can be readily studied with more reliability and ease than chronic toxicity testing for anticarcinogenic effect. Preliminary studies with metyrapone, which inhibits some forms of P-450, reveal that this compound completely inhibits the localization of ^{14}C-NNN in respiratory epithelium. The intriguing possibility that simple compounds may prevent the localization and hence carcinogenic action prompts the search described in this project. Inhibitors such as nicotine, ethanol, caffeine, dietary constituents, pyrazole, disulfiram, diethyldithiocarbamate, allyl alcohol, pregnenolone-16α-carbonitrile, selenium, progesterone (and other steroids), methotrexate, cycloleucine, methionine, 6-aminonicotinamide, nicotinamide, ascorbic acid, retinoic acid, BHA, vitamin E, pilocarpine, CoCl$_2$, and other constituents of sidestream smoke will be given to mice prior to the administration of ^{14}C-NNN. The mice will be studied by whole-body autoradiography to determine the extent to which the inhibitor blocks the accumulation of reactive metabolites of NNN. Histochemical and enzymatic studies will attempt to correlate the metabolism of NNN in these tissues with the retention of radioactivity.

Results to Date:
Results are not yet available.
Project Dates:
August 1981--July 1983.
Financial Support:
KTHRI (124-05-98902-4C040).

0936. UNIVERSITY OF LOUISVILLE, Department of Pharmacology and Toxicology, Health Sciences Center, Louisville, Kentucky 40292.

Project Title:
Inhibition of Localization of Tobacco Smoke Carcinogens in Sites of Tumor Formation.

Principal Investigators:
Waddell, W.J.; Marlowe, C.
Objective:
To fully characterize the mechanism of inhibition by ethanol and certain congeners in alcoholic beverages of accumulation of nitrosonornicotine (NNN) in some sites where tumors are usually produced, so that it can be controlled.
Methods or Approach:
Earlier research showed that metabolites of NNN localize precisely in sites where tumors appear, including nasal epithelium, salivary gland ducts, esophagus, liver, and bronchial epithelium. Since there is a specific affinity for these sites, it appeared likely that compounds could be found to block this localization. Nitrosamines, labeled with ^{14}C, will be injected into mice and mice will be sacrificed by freezing in hexane/dry ice at various time intervals. Animals will be processed by whole-body autoradiography for water-soluble compounds to identify tissues that retain radioactivity. To screen for potential blockers of this localization, selected compounds will be administered to mice. After the compound has been allowed to equilibrate, ^{14}C-nitrosamines will be injected and mice processed for whole-body autoradiography. Measurements of the photometric densities in whole-body autoradiographs will allow quantitation of localization of radioactivity in target tissues.
Results to Date:
A systematic search for potential blocking agents of NNN localization in epithelial tissues revealed that the usual pathways of demethylation and transmethylation were not involved; however, it was discovered that alcohols would block accumulation. Some alcohols found in commonly ingested beverages, were more potent than others, suggesting a specific enzymatic interaction. Findings indicate that an enzyme present in target tissues has a high enzymatic activity toward alcohols and nitrosamines and pretreatment with the alcohols might have great practical importance in preventing cancer from nitrosamines.
Future Plans:
It is anticipated that the technique of histochemistry will be combined with autoradiography, which will allow identification of cellular and subcellular sites that are alkylated by carcinogenic nitrosamines.
Project Dates:
August 1983–July 1985.
Financial Support:
Pharmacon Research Foundation, Inc.

0937. UNIVERSITY OF LOUISVILLE, SCHOOL OF MEDICINE, Department of Microbiology and Immunology, Room 410, Building 55A, Louisville, Kentucky 40292.

Project Title:
Effect of Passive Exposure to Cigarette Smoke on Membrane Glycoprotein Biosynthesis.

Principal Investigator:
Hunt, L.A.
Objective:
To identify and characterize specific alterations in cellular glycoprotein and polypeptide biosynthesis that result from direct exposure of murine cells in culture to sidestream cigarette smoke.
Methods or Approach:
Specific alterations are being compared with molecular alterations resulting from exposure to mainstream smoke or pure components of cigarette smoke to determine which major individual components are responsible for alterations in synthesis of certain proteins. Also, conditions of sidestream smoke exposure will be manipulated to determine the effect on protein alterations and to compare smoke-induced alterations with "cell stress/heat shock" proteins reported for many eukaryotic cell systems. Monolayer cultures of mouse L292 or B16 cells are exposed to different numbers of puffs of freshly generated sidestream or mainstream cigarette smoke, using a peristaltic pump-driven smoke apparatus. Following exposure, cell cultures are radiolabeled overnight with (^{3}H)-leucine (to label total newly synthesized cell protein) or (^{3}H)-mannose (to label newly synthesized cell glycoproteins). At the end of the labeling period, cell viability is determined on parallel cultures, and amounts of radiolabel incorporated into protein/glycoprotein are determined for each cell culture. Alteration in the level of synthesis of specific polypeptides or glycoproteins is determined by SDS-polyacrylamide gel electrophoresis and fluorography; specific alterations are quantitated by densitometer scans of gel profiles. Additional analysis of the carbohydrate side chains of cell glycoproteins utilizes the combined methodologies of gel filtration, lectin-affinity chromatography, and specific glycosidase digestions.
Results to Date:
Exposure of mouse B16 and L929 cell cultures to increasing numbers of puffs or sidestream cigarette smoke resulted in decreases in cell viability and corresponding decreases in levels of polypeptide and glycoprotein biosynthesis. A selective decrease in synthesis of a major cell membrane glycoprotein of approximately 46,000 mol wt was observed, along with the appearance of a new glycoprotein of approximately 58,000 mol wt. Alterations in the relative amounts of complex, acidic-type vs. high-mannose, neutral-type oligosaccharide chains on glycoproteins were also observed. Smoke exposures that resulted in approximately 30 to 40 percent loss in cell viability increased the relative amount of radiolabel in cell stress/heat shock-like polypeptides of 88,000, 66,000, and 23,000 mol wt. Higher dosages led to increased synthesis of 38,000, 45,000, and 30,000 mol wt proteins that have been tentatively designated as "cell death proteins." Mainstream smoke exposure led to similar polypeptide and protein alterations, and high concentrations of nicotine increased the labeling of a 70,000 mol wt protein.
Future Plans:
Plans are to continue analysis of the effects of smoke components on protein synthesis in mouse tissue culture cells and to further analyze and compare the smoke-induced proteins with authentic cell stress/heat shock proteins induced

by thermal stress. In addition, an attempt will be made to fractionate freshly generated smoke (gas phase vs. particulate phase) and manipulate the smoke by time delays or charcoal filters prior to exposure to cell cultures.

Project Dates:
July 1982–June 1984. KTHRI (KTRB-4CO43).

0938. UNIVERSITY OF LOUISVILLE, SCHOOL OF MEDICINE, Health Sciences Center, 500 South Preston, Louisville, Kentucky 40292.

Project Title:
Pilot Study to Screen Smokers Over 40 For Oral Cancer.

Principal Investigator:
Moore, C.

Objective:
To (1) determine feasibility of using an examination procedure on smokers over age 40 as a screening procedure, preliminary to planning a larger screening project; (2) examine degrees of accrual, acceptance, compliance, and attrition; and (3) determine feasibility of teaching the procedure to dentists.

Methods or Approach:
A large, randomized trial (at least 20,000 persons) would be needed to yield significant numbers of head and neck cancers, which would entail problems of accession, compliance, attrition, logistics in examining person, training of examiners, accomplishing examinations, and cost. Therefore, a pilot project was proposed to study accession, compliance, and attrition rates of study subjects and controls and to test feasibility of teaching dentists to accomplish oropharyngeal cancer examinations. The pilot also was designed to evaluate quality and efficacy of the examination as a screening procedure and test logistics of carrying out examinations expeditiously in dental offices. A computer printout of members (over 40 years of age) of a health maintenance organization serving industrial workers and their families in Louisville (8,000) was obtained, and smokers identified by card survey (2,700). Agreement to participate was requested of 200 randomly selected subjects and 200 controls, matched for sex and age. Dentists were taught to carry out oral cancer examinations and examined study participants twice/year for 1 year. The screening examination consisted of (1) targeted oral soft tissue examinations by inspection and palpation, and (2) oropharyngeal and laryngeal examination with Stortz rigid fiberoptic scope.

Results to Date:
Current smokers are less likely to accept and comply than exsmokers. Examinations of 77 smokers over age 40 (many undergoing a second exam 6 months later) showed that the procedure is feasible, teachable, and efficient. It can be done in a short period of time at low cost and with good patient acceptance. Preliminary data also indicate that response to the initial question was about 50 percent; acceptance of plan was <40 percent; compliance was about 70 percent of those accepting; and attrition was 40 percent. Very few current smokers were actually willing to go through two examinations.

Future Plans:
Data will be used to design a screening study for oropharyngeal cancer in smokers over age 40.

Project Dates:
July 1984–June 1985.

Financial Support:
NIDA.

0939. UNIVERSITY OF LOUISVILLE, SCHOOL OF MEDICINE, Department of Microbiology and Immunology, Louisville, Kentucky 40292.

Project Title:
Effect of Passive Exposure to Cigarette Smoke on Interferon Production.

Principal Investigator:
Sonnenfeld, G.

Objective:
To (1) determine if tobacco smoke can affect production of interferon, an important molecule for defenses against respiratory diseases and cancer; (2) determine if there are differences in effects of passive (sidestream) and active (mainstream) smoke; and (3) examine carcinogenic components of smoke for effects on interferon induction.

Methods or Approach:
A peristaltic pump smoking machine has been modified for exposing mice and tissue samples to mainstream and sidestream smoke. Tissue cultures or mice are placed in the chamber, exposed to smoke, and removed. Tissue cultures are examined for possible toxic effects, and carboxyhemoglobin determinations are made on mice. Cultures or mice are then challenged with polyriboinosinic-polyribocytidylic acid to produce interferon-alpha/beta or phytohemagglutinin to produce interferon-gamma. Interferon samples are then harvested and assayed for antiviral activity. In addition, cultures or mice are exposed to carcinogenic components of tobacco smoke such as benzo(*a*)pyrene (BaP). After appropriate exposure, mice or cultures are induced to produce interferon and assayed for interferon activity.

Results to Date:
Results indicate that both sidestream and mainstream smoke can affect viability of cultured L-929 cells. Toxicity can be moderated by smoke dilution, passage of smoke through activated charcoal, and aging of smoke (delaying time of cell exposure after smoke generation). Preliminary data indicate that there are some effects of exposure on interferon production by cells and whole mice. Carcinogenic components of cigarette smoke, such as BaP, also appear to inhibit interferon production; however, this result does not appear to be related to toxic effects of BaP, since it is completely reversible. In addition, BaP requires activation to the ultimate carcinogenic form by liver microsomal enzymes. Interferon induction or passive transfer to mice inhibits this activation, suggesting a possible regulatory circuit among interferon, micosomal enzymes, and carcinogens.

Future Plans:
Studies will be extended to include a comprehensive examination of effects of mainstream and sidestream smoke on in vivo interferon-alpha/beta and interferon-gamma production; (2) examination of specificity of effects to interferon system, or whether effects can be seen with other induced proteins; and (3) smoke and cigarette manipulations to determine if effects of smoke exposure can be lessened.

Project Dates:
July 1981–June 1987.

Financial Support:
KTHRI.

0940. UNIVERSITY OF LOUISVILLE, SCHOOL OF MEDICINE, Department of Family Practice, Louisville, Kentucky 40802.

Project Title:
Acupuncture Therapy for the Treatment of Tobacco Smoking Addiction.

Principal Investigators:
Steiner, R.P.; Hay, D.L.; Davis, A.W.

Objective:
To evaluate acupuncture treatment effect on cigarette smoking habit with a motivated population in a controlled clinical setting.

Methods or Approach:
From a volunteer research population, 16 matched pairs were assembled according to age, sex, and severity of smoking habit. Research subjects were randomly assigned to real or sham acupuncture treatment groups. Self-reported cigarette smoking logs were measured pre- and posttreatment. Analysis of variants confirmed homogeneity of group pretreatment cigarette consumption.

Results to Date:
Cigarette consumption decreased significantly in both real and sham treatment groups. Treatment group, age, sex, or severity of smoking habit were not significant factors in treatment effects for cessation of smoking. Legitimate crossover treatment for sham research group showed a significant decrease ($p \leq 0.05$) in cigarette consumption; however, this change was not statistically different from change in consumption during placebo treatment. It is concluded that acupuncture did not enhance cessation of smoking in this study population.

Future Plans:
Unpublished measures of acupuncture meridian energetic status indicate that balancing meridian forces according to the traditional model may not have been accomplished in treatment protocol. Also, the short treatment period may not have been sufficient to overcome social pressures, common reinforcements, and cues for smoking behavior. Further research is planned to resolve these issues.

Financial Support:
University of Louisville.

Reference:
Steiner, R.P.; Hay, D.L.; Davis, A.W. "Acupuncture Therapy for the Treatment of Tobacco Smoking Addiction." *American Journal of Chinese Medicine* 10(1/4):107-121, 1982.

0941. UNIVERSITY OF LOUISVILLE, SCHOOL OF MEDICINE, Department of Pharmacology and Toxicology, Louisville, Kentucky 40292.

Project Title:
Characterization of the Nicotine-Induced Stimulation of Cholinergic and Dopaminergic Activity in the CNS.

Principal Investigators:
Rowell, P.P.; Carr, L.A.

Objective:
To analyze effects of nicotine exposure (chronic, acute, and in vitro effects) on dopaminergic activity in the nucleus accumbens and amygdala; elucidate neurochemical effects of long-term cigarette smoking.

Methods or Approach:
Available evidence indicates that nicotine's effect is produced by increasing release of monoamine neurotransmitters, the most likely candidate being dopamine. Male Sprague-Dawley rats will be divided into two groups: untreated animals and animals chronically treated with nicotine in drinking water (40 μg/mL). After 3 to 6 months, animals from both groups will be sacrificed and brains removed. Slices will be prepared from specific locations, and brain areas needed will be separated from slices. Characterization of dopamine and acetylcholine release will be performed, using a superfusion method that allows rapid addition or removal of nicotine or other drugs. Also, conditions of the medium can be changed at various time intervals during the experiment. Effect of attenuation of nicotine-induced release in chronically treated animals will be investigated and comparisons will be made between animals from the treated and untreated groups. Effect of acute nicotine administration in vivo 30 minutes prior to sacrifice on nicotine-induced release will be studied to differentiate between a biochemical mechanism of tolerance and a pharmacokinetic drug interaction. In vitro effects of acute and chronic nicotine exposure on activity and kinetics of dopamine uptake and tyrosine hydroxylase will also be investigated.

Results to Date:
Nicotine stimulates release of ^{3}H-dopamine in isolated striatal nerve endings. A system for kinetically analyzing release of transmitter at 1-minute intervals by superfusion was developed because of the magnitude and time course of the nicotine-induced release. One of the most interesting findings to date is that chronic nicotine exposure significantly depresses acute effects on transmitter release. Since nicotine-induced release is localized to the presynaptic nerve terminal, an investigation of tolerance to nicotine's actions brought about by long-term nicotine exposure is examining neurochemical changes that occur in localized synaptic areas rather than in the brain as a whole.

Future Plans:
Studies will center on changes in receptors that may occur as a result of nicotine exposure. Comparisons will be made between in vitro nicotine and chronic and acute nicotine administration. Receptor kinetics of specific saturable binding, using dopaminergic receptor ligands, will be determined.

Project Dates:
July 1984–June 1987.

Financial Support:
KTHRI.

0942. UNIVERSITY OF LOUISVILLE, BELKNAP CAMPUS, SCHOOL OF MEDICINE, Exercise Physiology Laboratory, Louisville, Kentucky 40292.

Project Title:
Cigarette Smoking, Exercise and High Density Lipoprotein Cholesterol

Principal Investigators:
Stamford, B.A.; Matter, S.; Fell, R.D., et al.

Objective:
To determine effects of smoking and exercise on blood lipids and lipoproteins in middle-aged males.

Methods or Approach:
Cigarette smoking is associated with depressed levels of high density lipoprotein cholesterol (HDL-C), whereas exercise is associated with elevated levels. It was hypothesized that smoking may attenuate effects of exercise to elevate HDL-C. Study population consisted of 269 males (70 smokers) who met all the criteria. Age, height, weight, body fatness (hydrostatic weighing), daily caloric consumption and alcohol intake, and smoking habits and history were determined. Interviews concerning physical activity patterns were conducted and cardiovascular responses to treadmill exercise were determined. Subjects were grouped as sedentary (low activity), participants in vigorous recreational activities (moderate activity), and joggers/runners (high activity). Analysis of covariance with adjustments for factors that may affect blood lipids and lipoproteins was employed.

Results to Date:
Smokers demonstrated lower HDL-C and higher total cholesterol levels than nonsmokers. High activity subjects demonstrated significantly higher HDL-C levels than low and

moderate groups, which did not differ. High activity smokers did not differ from low activity nonsmokers with respect to HDL-C, which supports the proposed hypothesis. Nonsmokers were higher in weight and body fatness than smokers even though smokers consumed an average of 288 more calories/day, suggesting that smoking may account for a significant number of calories through altered metabolism or some other means.

Financial Support:
AHA; University of Kentucky.

Reference:
Stamford, B.A.; Matter, S.; Fell, R.D., et al. "Cigarette Smoking, Exercise and High Density Lipoprotein Cholesterol." *Atherosclerosis* 52:73-83, 1984.

0943. USDA, ARS, UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Minor Alkaloids of Tobacco.

Principal Investigators:
Bush, L.; Hamilton, J.; Chaplin, J.F.

Objective:
To determine accumulation of alkaloids in root and leaf tissue including cured leaf of burley and flue-cured tobacco and *Nicotiana* species.

Methods or Approach:
Field and greenhouse plants of flue-cured and burley tobacco will be produced. Lines with varying levels of total alkaloids and certain species will be used with nornicotine producing lines. Tissue will be analyzed at various steps of growth and after curing for nicotine, nornicotine, anabasine, anatabine, myosmine, 2,3'bipyridyl, cotinine, N'-isopropylnornicotine, and N-nitrosonornicotine. Synthesis and conversion of constituents will be related to time of plant development.

Results to Date:
Results are not yet available.

Project Dates:
June 1982–December 1984.

Financial Support:
USDA (7016-20881-024-A).

0944. USDA, ARS, UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Accumulation of Burley Tobacco Health-Related Constituents: Effect of Slow-Release Fertilizers.

Principal Investigators:
MacKown, C.T.; Sims, J.L.

Objective:
To determine effect of slow-release nitrogen fertilizer on health-related chemical constituents, growth, and yield of burley tobacco; evaluate effect of slow-release nitrogen (N) fertilizers on N use efficiency.

Methods or Approach:
Replicated experiments will be conducted in field and greenhouse studies. Selected nitrogen sources with different rates of release will be used in field studies; slow-release sources will be compared with equivalent applications of water-soluble nitrogen fertilizers, urea, and calcium nitrate. Crop growth, chemical composition, soil inorganic nitrogen levels, and soil pH will be determined throughout the growing season and harvested plants will be analyzed for selected chemical components. After the first year, experiments may be modified to study effect of split applications and combinations of slow-release and water-soluble nitrogen fertilizer. Replicated greenhouse experiments complementing field experiments will be conducted. Both plants and soil will be sampled over time. Partitioning of nitrogen constituents and measurements of soil pH and available nitrogen will be determined.

Results to Date:
Results are not yet available.

Project Dates:
June 1982–June 1985.

Financial Support:
USDA (7018-2881-026-A).

0945. USDA, ARS, UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Effect of Cultural Practices on N'-Nitrosonornicotine Content in Tobacco.

Principal Investigators:
Davis, D.L.; Sims, J.L.; MacKown, C.T.

Objective:
To determine effects of nitrogen (N) management, leaf constituents, and curing environment on N'-nitrosonornicotine content in burley tobacco leaves.

Methods or Approach:
To determine the N'-nitrosonornicotine content of four burley genotypes (ranging from low to high total alkaloid concentration) grown under seven different N management treatments. Measure formation of N'-nitrosonornicotine during incubation of homogenized tobacco leaves. Evaluate the effects of microbial inhibitors and nitrite additions on N'-nitrosonornicotine formation during incubation of homogenates. Analyze air-cured and homogenized leaf-cured tobacco for related chemical constituents. The four burley 21 isolines investigated were burley 21, LA B21, LIA B21, and HN B21. The seven N treatments involving rates and times of application were (in kg/ha): 0, 280 at transplant, 280 mid growth, 280 at topping; 140 transplant/140 mid, 140 transplant/140 top, and 140 mid/140 top.

Results to Date:
Yield ranged from 1,776 to 3,379 kg/ha; crop value differences coincided with genotype and N management. Total alkaloids ranged from 0.23 to 4.59 percent. Lamina alkaloid concentrations are similar to previously reported levels for each of the breeding lines. Total alkaloid concentration was less in the check than in the plots receiving N; however, the N management schemes were not different. The greatest nicotine concentration was from treatments receiving all of the N prior to topping or at least one-half during midseason. Lamina nitrate N ranged from 580 to 7432 ppm. Nitrate concentration was lowest in the LIA B21 line and highest in the nornicotine B21. N management schemes had significant impact on lamina nitrate N concentration; nitrate N level was lowest in the check (1610 ppm) and highest in the 280 kg N/ha application following transplanting. Extractions of 2R1 reference tobacco have been analyzed for tobacco-specific nitrosamines by gas chromatography with a thermal energy analyzer detector.

Project Dates:
June 1981–August 1984.

Financial Support:
USDA (7014-20881-022S).

0946. USDA, ARS, UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Nitrogen and Potassium Effects on Health Related Constituents of Burley Tobacco.

Principal Investigators:
Sims, J.L.; Grove, J.H.; Chaplin, J.F.
Objective:
To determine nitrogen (N) and potassium (K) interactions on levels of health-related constituents of burley tobacco; determine influence of N and K and the source of K on soil colloid and solution chemistry controlling K supply to plants.
Methods or Approach:
Replicated field trials will be conducted. Treatments include 100, 200, 300, and 400 lb N/acre as ammonium nitrate and 0, 100, 200, and 400 lb K/acre as chloride and sulfate. Molybdenum will be added in transplant water at 0.5 lb sodium molybdenate. Soil analyses before fertilization and at transplant will include electrical conductivity (ions of K, calcium, magnesium, sodium, ammonium, nitrate, chloride, and sulfate in soil solution), exchangeable cations, and soil pH. Soil will be characterized for K capacity and intensity relationships. Above-ground plant parts will be taken at 4, 8, and 12 weeks for weight and chemical analyses. Plants will be harvested at maturity, air-cured, and processed for yield, value, and leaf analysis. Tissue will be analyzed for mineral cations and anions; cured leaf will be analyzed for total N, nitrate N, protein N, total alkaloids, burn, solanesol, carotenoids, and total particulate matter.
Results to Date:
Project is in a preliminary phase.
Project Dates:
June 1983–June 1985.
Financial Support:
USDA (7020-20881-028S).

0947. USDA, ARS, UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Modification of Tobacco Leaf Components Using Selected Microorganisms in Homogenized Leaf Curing.

Principal Investigators:
Taraba, J.L.; Yoder, E.E., Spurr, H.W., Jr.
Objective:
To determine effects of naturally occurring and introduced microorganisms on homogenized leaf-curing process for the purpose of decreasing chemicals from tobacco leaves that have potential risks to health.
Methods or Approach:
Natural microflora of tobacco leaves will be altered by chemical additives and/or by introduction of other microorganisms. Tobacco leaves will be processed using homogenized leaf-curing methodology and the impact of the microorganisms and alterations in microbial populations will be assessed in relation to the curing process, chemical quality of the product, and the health risk of the resulting product.
Results to Date:
Results are not yet available.
Project Dates:
June 1982–June 1985.
Financial Support:
USDA (7019-20881-027A).

0948. USDA, ARS, UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Insecticide, Genotype and Plant Development Influence on Tobacco Tar and Chemical Constituents.

Principal Investigators:
Thurston, R.; Jones, G.; Davis, D.L.
Objective:
To determine effect of insecticides, genotypes, and plant development on levels of tar and other health-related leaf components, especially nitrogenous constituents.
Methods or Approach:
Acetate, methomyl, carbaryl, and carbofuran will be applied to tobacco, and effects on rate of growth and maturation will be determined. Total particulate matter index (PMI) and nitrogenous constituents including nitrates, protein nitrogen (N), total nitrogenous bases, and α amino N will be determined. PMI determinations will be made on Tobacco Introductions, several *Nicotiana* species, and F_1 hybrids.
Results to Date:
Range in PMI in Tobacco Introductions (1,168) was from 136 mg/g to 294 mg/g; range for nicotine from pyrolyzed samples was from <1.0 mg/g to >35 mg/g, indicating considerable variation, which can be used in changing these characteristics in tobacco. Of the pesticides tested (disulfoton, carbofuran, acephate, methomyl, carbaryl, and metalaxyl), none affected the chemical components of cured leaf, measured by total N, nitrate N, total alkaloids, petroleum ether extract, calcium, phosphorus, and potassium. Metalaxyl (systemic fungicide) was used in transplant water, as a foliar spray, and in combination treatments with maleic hydrazide (MH, a systemic sucker control agent). Residue levels of metalaxyl ranged from 0 to 101 mg/g in cured leaf. Residue levels were greater from foliar applications of metalaxyl near harvest time and lowest when applied as preplant-incorporated or transplant water treatment. Application of metalaxyl did not alter MH residues when applied as a combination treatment. Studies of tobacco grown hydroponically in nutrient solution indicated that rate of uptake was proportional to plant growth and that metalaxyl was translocated from older plant parts to new growth.
Project Dates:
June 1979–June 1983.
Financial Support:
USDA (7003-20881-008S).

0949. USDA, ARS, UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Effect of Homogenized Leaf Curing and Protein Extraction on Chemical Composition of Processed Tobacco.

Principal Investigators:
Yoder, E.E.; Lowe, R.H.; Burton, H.E.
Objective:
To develop techniques for extracting protein from tobacco leaves that are compatible with homogenized leaf curing methods; continue evaluation of homogenized leaf curing in relation to producing tobacco that has improved usability, particularly with respect to consumer safety.
Methods or Approach:
Burley tobacco will be grown and harvested by conventional means to furnish fresh leaf material for processing by homogenized leaf curing. After a two-stage grinding operation, tobacco will be subjected to a variety of treatments involving incubation

at selected temperatures and sparging rates. Effects of mechanical dewatering will be tested in connection with protein extraction. Tobacco will be dried either by convective type method (fluidized bed system) or by conductive type method (moving stainless steel belt). Tobacco samples will be soaked and condensate analyzed for chemical constituents; short-term bioassays will determine usability of tobacco material. Homogenized leaf cured (HLC) tobacco was processed for storage investigations. Incubation at 40° C involved three lines (Ky-14, high alkaloid B-21, and nornicotine converter), two levels of additives (ascorbic acid and no additives), and six times (0, 4, 8, 12, 20, and 25 hours). Samples of incubated tobacco were frozen after removal from the incubator and stored until dried. Research was conducted to assess microbial activity that occurred during incubation of burley tobacco.

Results to Date:

Preliminary data show that 70 percent of isolates of HLC tobacco were gram-positive cocci (staphylococci) rather than gram-positive rods of *Lactobacillus* and *Bacillus* that are found in conventional air-cured tobacco. It was concluded that altering natural microflora of HLC tobacco with a selected inoculum may allow final chemical concentrations to change. Ozone was applied in pilot-size equipment to burley and flue-cured slurries. Results confirm feasibility of the procedure for modification of chemical constituents by treatment with ozone. A strategy to reduce unit amortization cost of HLC post-harvest processing equipment may be to hold tobacco received during the short 5- to 6-week harvest period in long-term unincubated slurry (9 to 10 months), thereby reducing investment for equipment for incubation, drying, and reconstitution. Frozen tobacco slurries (-20° F) remain sufficiently microbially inert during long-term storage for subsequent HLC processing.

Project Dates:

May 1978–July 1983.

Financial Support:

USDA (7005-20830-014S).

Reference:

Anderson, R.; Kasperbauer, M.; Burton, H., et al. "Changes in Chemical Composition of HLC and Air-Cured Burley Tobacco Stored in Controlled Environment." *Journal of Agricultural and Food Chemistry* 30:663-668, 1982.

0950. USDA, ARS, UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:

Health Related Chemical Analyses of Tobacco Leaf.

Principal Investigators:

Burton, H.R.; Leggett, J.E.

Objective:

To (1) conduct chemical analysis of tobacco plant tissue as required by all tobacco and health investigators; (2) improve and expand present analytical procedures; and (3) develop new methods for oxidation and degradation products of carotenoids.

Methods or Approach:

Approximately 60,000 samples from various tobacco and health projects will be analyzed for chemical components as determined by project leaders and laboratory director. Analyses include alkaloids, total nitrogen, nitrate, protein, volatile bases, ammonia, reducing sugars, calcium, magnesium, potassium, phosphorus, moisture, ash, and alkalinity. Routine analyses, using high pressure liquid chromatography and gas chromatography for oxidation and degradation products of carotenoids, will be developed.

Results to Date:

Approximately 75,000 separate analyses were made for tobacco researchers during the past year, in addition to analyses performed by individual investigators. Analyses included total alkaloids, nitrate, nitrite, total nitrogen, protein nitrogen, total volatile nitrogen bases, total reducing substances, petroleum ether extractables, neophytadiene, individual hydrocarbons, total hydrocarbons, chlorophyll a, chlorophyll b, carotene, lutein, neoxanthin, violaxanthin, nicotine, nornicotine, anabasine, potassium, calcium, phosphorus, sulfur, magnesium, sodium, and minor elements. Burley tobacco was field grown and cured for investigating changes in pigment levels during curing. Selected samples will be analyzed for solanesol and volatile degradation flavor constituents. Procedures are being modified for chemical analyses of solanesol and volatile carotenoid degradation products in tobacco leaf.

Project Dates:

June 1981–June 1984.

Financial Support:

USDA (7003-20882-005S).

0951. USDA, ARS, UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:

Microbial Reduction of Nitrate and Production of Nitrite in Tobacco.

Principal Investigators:

Smith, M.S.; Hamilton, J.L.; Chaplin, J.F.

Objective:

To determine mechanisms for controlling rate of bacterial nitrate reduction and nitrite accumulation in homogenized leaf curing and air curing of burley tobacco.

Methods or Approach:

Population changes of various types of nitrate (NO_3)-reducing bacteria before, during, and after curing were determined, and effects of microbial antibiotic treatments on NO_3 reduction and nitrite (NO_2) production were observed. Effects of pH, temperature, and aeration during incubation on denitrification and microbial reduction of NO_3 were evaluated. Predominant genera were identified after 30 to 40 individual isolates of NO_3-reducing bacteria were characterized. After heat sterilization of leaf slurries or extracts to reduce native bacterial populations, isolated denitrifying bacteria were inoculated under various atmospheric conditions to determine optimal reduction of NO_3 during incubation.

Results to Date:

Rates and products of nitrate reduction were measured in air cured, homogenized leaf cured (HLC), and tobacco filtrates. Evidence of a significant role of microbes, evaluation of parameters controlling NO_2 accumulation, and approaches to manipulation of NO_3 and NO_2 in tobacco were tested. With high levels of leaf nitrite, growth of nitrate respirers were observed; when no nitrite accumulated in leaf, little or no growth was obtained. Inconsistency of data and failure of procaryotic inhibitor (streptomycin) to affect leaf NO_2 content make it impossible to be certain of the role of nitrate-respiring bacteria. Slurries exhibited much clearer relationships between nitrate-respiring bacteria and nitrate and nitrate concentrations. Nitrate accumulation was shown to be microbial by effect of procaryotic antibiotics, the lag phase followed by an exponential phase of nitrite reduction or nitrite accumulation in filter-sterilized extracts. Acidity appears to be important in accounting for NO_2 accumulation. HLC pH allows relatively rapid NO_3 reduction to NO_2, but is too acidic for optimal denitrification of NO_2 to N gas. Three *E. coli* mutants, lacking

NADH-dependent nitrite reductase, produced N_2O at rates equal to the wild type. Observations suggest that N_2O is produced enzymatically, but not by the same enzyme system responsible for dissimilatory reduction of NO_2 to ammonium ion.

Project Dates:
June 1981–June 1984.

Financial Support:
USDA (7013-20881-021S).

References:
(1) Parsons, L.L. "Microbial Reduction of Nitrate and Production of Nitrite in Tobacco During Curing." Master's Thesis, University of Kentucky, Lexington, 1984. (2) Smith, M.S. "Dissimilatory Reduction of NO_2 to NH_4 and N_2 by a soil *Citrobacter sp.*" *Applied Environmental Microbiology* 43:854-860, 1982. (3) Smith, M.S. "Nitrous Oxide Production by *Escherichia coli* Is Correlated With Nitrate Reductase Activity." *Applied Environmental Microbiology* 45:1545-1547, 1983.

0952. USDA, ARS, UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Moisture Content During Storage on Health-Related Properties of Burley Tobacco.

Principal Investigators:
Walton, L.R.; Henson, W.H., Jr.; Casada, J.H.

Objective:
To (1) determine physical and chemical properties of burley tobacco during storage of bales and tied bundles as a function of leaf moisture and time of storage; (2) compare physical and chemical properties to level of properties entering storage; (3) monitor and mathematically describe migration of moisture in densely packed leaves during storage; and (4) relate changes in alkaloids to safety and health.

Methods or Approach:
Bales and tied bundles of burley tobacco at 16 to 18 percent, 20 to 22 percent, and 24 to 26 percent moisture content (w.b.) will be stored for 12 months. Tobacco quality going into storage and at various stages of storage will be determined by visual inspection for physical condition and by sampling for chemical constituents and microorganism activity. The mathematics of the simultaneous heat and mass transfer process taking place in the tobacco will be developed using both analytical and computer techniques. Vapor diffusivity will be evaluated for use in the mathematical model. The model and results of the storage experiment will be used to predict allowable moisture content for marketing, short-term storage, long-term on-farm storage, and drying of high-moisture bales and bundles for storage.

Results to Date:
Particulate matter index (PMI) declined by about one-fourth of original value over 7 months of storage. Neither moisture content nor package (bales or bundles) had an effect on PMI. Total alkaloids declined during storage with magnitude of reduction increasing with increasing moisture content. Maximum reduction in nicotine was about one-fifth of its original value, indicating that fermentation occurred during storage. Total nitrogen increased during storage, but was not affected by moisture content. Protein nitrogen increased, with the greatest increase occurring at high moisture level. Soluble nitrogen was unchanged. Nitrate nitrogen and petroleum ether extract increased with time, but were unaffected by moisture content. The diffusion model for the bale showed weight loss per bale due to moisture loss after a 12-month period to be 0.2 kg at low moisture, 2.4 kg at normal moisture, and 5.0 kg at high moisture. For high-moisture bales at both temperature levels, bacterial populations rose approximately two orders of magnitude to 10^8 to 10^9 cfu/g DM while bundles remained constant or decreased. Mold populations decreased two orders of magnitude, from 10^5 to 10^3 cfu/g DM. Dry weight loss was 4.6 percent, 5.7 percent, and 7.3 percent at low, normal, and high moisture, respectively. Storage of high moisture burley in the bale will incur mild fermentation that accelerates chemical changes that normally occur during natural aging.

Project Dates:
July 1980–December 1982.

Financial Support:
USDA (7007-20881-015S).

Reference:
Swetnam, L.D.; Walton, L.R. "Moisture Diffusivity of Densely Packed Cured Burley Tobacco." *Transactions of American Society of Agricultural Engineers* (In press).

0953. USDA, ARS, UNIVERSITY OF KENTUCKY, Lexington, Kentucky 40506.

Project Title:
Soil Water Stress on Growth Assimilation, Partitioning of C and N in Tobacco.

Principal Investigators:
Phillips, R.E.; Leggett, J.E.; Chaplin, J.F.

Objective:
To determine effects of soil water stress on assimilation and partitioning of carbon and nitrogen in tobacco, tar and nicotine delivery, and compounds such as solanesol, chlorogenic acid, and nitrosamines.

Methods or Approach:
Field experiments will be conducted to determine effects of soil water stress on growth, yield, and chemical composition. Samples will be obtained at various stages of growth: 35 to 40 days after transplanting, at topping, 15 days after topping, harvest, and cured. All plants will be separated into lamina, midvein, and stalk and analyzed for total nitrogen, free amino acids, nitrate, protein, organic acids, total carbohydrates, soluble carbohydrates, starch, tar, alkaloids, solanesol, chlorogenic acid, and nitrosamines.

Results to Date:
Results are not yet available.

Project Dates:
June 1982–June 1985.

Financial Support:
USDA (7017-20881-025-A).

0954. VETERANS ADMINISTRATION MEDICAL CENTER, Leestown Road, Lexington, Kentucky 40507.

Project Title:
Smoking Effect of Lipoprotein Levels and Vascular Diseases.

Principal Investigators:
Mandelstam, P.

Objective:
To (1) ascertain whether cessation of smoking results in changes in serum cholesterol-binding reserve and in plasma lipoproteins (especially high density lipoproteins) and whether resumption of smoking has any effect; (2) determine whether or not smokers have altered serum cholesterol-binding reserve and altered plasma lipoproteins (especially high density lipoproteins) compared with nonsmokers and ex-smokers; (3) determine whether cigarette smoking influences frequency and severity of diabetic retinitis; and (4) study the interrelation-

ships between cigarette smoking, frequency and severity of diabetic retinitis, and levels of plasma lipoproteins and cholesterol-binding reserve.

Methods or Approach:
For lipoprotein and cholesterol, four groups will be studied: (1) patients free of vascular disease, (2) those with coronary artery disease, (3) those with peripheral arterial disease, and (4) those with carotid artery disease. Plasma will be utilized for lipoprotein electrophoresis and for preparative ultracentrifugation for separate analysis of high density, low density, and very low density lipoproteins by standard methods. Cholesterol and triglyceride will be analyzed by standard methods and cholesterol-binding reserve by the method of Hsia.

Results to Date:
Since July 1982, 170 patients with peripheral arterial disease have been examined.

Financial Support:
VA.

0955. VETERANS ADMINISTRATION, Leestown Road, Lexington, Kentucky 40511.

Project Title:
Effect of Surgical Treatment on Cutaneous Blood Flow in the Feet of Patients With Symptomatic Atherosclerotic Disease.

Principal Investigators:
Hyde, G.L.; Richardson, D.

Objective:
To determine the effects of aging, smoking, and atherosclerotic disease on microcirculation.

Methods or Approach:
Cutaneous microcirculation in the great toe nailfold in 20 atherosclerotic patients was compared with 10 age-matched controls and 10 young control subjects. A system of videomicroscopy was used that employed a microscope, camera, television monitor, videorecorder, and video densitometry equipment to calculate the velocity of capillary blood flow.

Results to Date:
The data demonstrate alterations of cutaneous microcirculatory blood flow mechanisms in the atherosclerotic patients as well as the inability of the microcirculation to increase capillary blood velocity and its attendant oxygen delivery capability in response to arterial flow perturbation. The altered capillary physiology may explain the etiology of dependent rubor and postreconstructive pedal edema.

Financial Support:
VA.

0956. WESTERN KENTUCKY UNIVERSITY, Department of Health and Safety, Bowling Green, Kentucky 42101.

Project Title:
Intrastate Production and Consumption of Tobacco As an Index of the Influence of Tobacco Growing on Individual Smoking Behavior.

Principal Investigator:
Wilson, R.W.

Objective:
To measure the size of tobacco crops in tobacco-producing states in proportion to population size and land area; compare data with statewide tobacco consumption.

Methods or Approach:
Data, retrieved from state departments of agriculture and commerce, include pounds of tobacco raised, total tobacco acreage, state population, and wholesale and retail sales figures for tobacco products.

Results to Date:
Results are not yet available.

Project Dates:
July 1984–June 1985.

Financial Support:
Western Kentucky University.

0957. WESTERN KENTUCKY UNIVERSITY, Department of Health and Safety, Bowling Green, Kentucky 42101.

Project Title:
A Survey of Smoking Related Attitudes and Behaviors Among Kentucky Public School Children, Parents, and Teachers.

Principal Investigators:
Higgins, C.W.; Dunn, J.D.; Warmack, D., et al.

Objective:
To determine if direct involvement with tobacco production influences smoking-related attitudes and behaviors among Kentucky public school children, their parents, and their teachers.

Methods or Approach:
Public schools in four counties in eastern Kentucky were randomly selected from a sampling frame containing all public schools in the area. The sample was stratified so that both primary and secondary schools were represented. All students and teachers were surveyed during regular school hours; parents were surveyed by take-home instruments to be returned by mail.

Results to Date:
Children, parents, and teachers who were directly involved in tobacco production were more likely to smoke, to have started smoking at a younger age, and to hold attitudes more favorable toward smoking and less favorable toward efforts to discourage smoking than persons not involved with tobacco production. The involved individuals were also less impressed by the health risks of smoking.

Future Plans:
College students will be surveyed to assess smoking-related attitudes and behaviors and the impact of involvement in tobacco production of receptiveness toward smoking education messages.

Financial Support:
Kentucky Department of Human Resources.

0958. LOUISIANA STATE UNIVERSITY SCHOOL OF MEDICINE, Department of Pediatrics, 1542 Tulane Avenue, New Orleans, Louisiana 70112. HARBOR-UCLA MEDICAL CENTER, Departments of Pediatrics and Pathology, Torrance, California 90502.

Project Title:
Immunoglobulin E Pattern in Cigarette Smokers.

Principal Investigators:
Bahna, S.L.; Heiner, D.C.; Myhre, B.A.
Objective:
To investigate the relationship between tobacco smoking and serum immunoglobulin E (IgE) level.
Methods or Approach:
Serum IgE levels in healthy blood donors who had no history of atopy were measured by a paper-disc radioimmunoassay and analyzed according to smoking habits.
Results to Date:
The IgE geometric mean for regular smokers was 41.7 IU/mL, significantly higher than in nonsmokers (19.3 IU/mL) or rare smokers (22.7 IU/mL); 28 percent of smokers had IgE levels >200 IU/mL. IgE levels in smokers showed a moderate inverse correlation with degree of smoking. The number of years of smoking did not seem to significantly influence IgE level. Mean IgE level in ex-smokers was much lower than in current light smokers but still higher than in nonsmokers. There was a moderate inverse correlation between IgE levels and duration of cessation of smoking. Data suggest a characteristic pattern for the influence of cigarette smoking on serum IgE level; a striking rise associated with light smoking and a remarkable drop in heavy smokers. Such changes seemed reversible after cessation. Smoking status, therefore, appears to be an important consideration in interpreting serum IgE levels and in revising "norms" of IgE levels.
Financial Support:
NICHHD (09327).
Reference:
Bahna, S.L.; Heiner, D.C.; Myhre, B.A. "Immunoglobulin E Pattern in Cigarette Smokers." *Allergy* 38:57-64, 1983.

0959. LOUISIANA STATE UNIVERSITY MEDICAL CENTER, NATIONAL RESEARCH AND DEMONSTRATION CENTER, ARTERIOSCLEROSIS, 1542 Tulane Avenue, New Orleans, Louisiana 70112-2822.

Project Title:
Early Natural History of Arteriosclerosis and Essential Hypertension: Biobehavioral Study of Cardiovascular Risk Factors in Children.

Principal Investigators:
Hunter, S.M.; Berenson, G.S.
Objective:
To (1) study early natural history of atherosclerosis and essential hypertension; (2) develop methods of intervention; (3) measure selected health habits or coping behaviors associated with development of coronary heart disease in adults; and (4) assess physiological consequences at an earlier age.
Methods or Approach:
Cigarette smoking and smokeless tobacco use were among the health habits studied. Longitudinal data on cigarette smoking behavior have been collected since 1976 on individuals aged 8 to 25. Cross-sectional and longitudinal trends in smokeless tobacco use have also been analyzed. Data on children were collected by self-administered questionnaire during regular screening of physiological risk factors. Parallel forms were developed and administered 2 weeks later to a random subsample to assess test–retest reliability. A synonym list was developed to insure standardized responses to word meaning questions. In third through sixth grade, questionnaires were read to the children from a tape recorder. As part of regular venipuncture performed for serum lipid analysis, an aliquot of blood was collected from each child and analyzed for plasma thiocyanate as an independent measure of smoking. For each survey, behavioral measures assessed with the quesionnaire were validated with blood samples.
Results to Date:
Responses to identical questions posed in the 1976-1977 and 1980-1981 screenings showed that although exposure has decreased, white males remain the leaders in earlier experimentation and regular smoking: 32 percent of those aged 14 and 15 indicated regular smoking in 1976 compared with 17 percent in 1980 (32 percent of those aged 16 and 17 reported smoking in 1980, similar to the number in 1976). Among white females, a decline in the number of regular smokers occurred in 16- to 17-year-olds (from 41 percent to 33 percent). Among black males, regular smoking decreased in both age groups (from 17 to 10 percent in those aged 14 and 15 and from 27 to 25 percent in those aged 16 and 17). For black females, initiation rates were similar in both surveys, but there was a decrease in nonsmoking behavior starting at age 12. A comparison of data from the two surveys showed that the prevalence of smokeless tobacco use increased in every age category, and was particularly dramatic in the snuff-dipping category where the increase was nearly threefold in all groups, although girls and blacks indicated little or no use of smokeless tobacco products.
Future Plans:
The interrelationships between type A behavior, coping strategies, genetics, and friendship networks with the adoption and use of tobacco products will be examined.
Project Dates:
December 1972–November 1986.
Financial Support:
NHLBI (HL15103-14).

0960. LOUISIANA STATE UNIVERSITY, 1901 Perdido Street, New Orleans, Louisiana 70112.

Project Title:
Case–Control Study of Cancer of the Lung, Stomach and Pancreas.

Principal Investigator:
Correa, P.
Objective:
To identify factors associated with the high cancer rates in Louisiana; determine the role of smoking, nutrition, occupation, and residential history.
Methods or Approach:
Cases and controls are identified in Louisiana, and a personal interview is carried out.
Results to Date:
Results are not yet available.
Project Dates:
June 1979–1983.
Financial Support:
NCI (NO1-CP-91023).

0961. LOUISIANA STATE UNIVERSITY, Department of Chemistry, Baton Rouge, Louisiana 70803.

Project Title:
The Toxicology of Cigarette Smoke.

Principal Investigators:
Pryor, W.A.; Church, D.F.
Objective:
To study toxicology of smoke and tar from environmental sources such as tobacco smoke; determine whether radicals in gas phase smoke are responsible for some of the toxicological effects of smoking.
Methods or Approach:
Techniques of the free radical chemist and biochemist are used, including kinetics and product analyses, studies of model reactions, and electron spin resonance and spin trap methods. Spin trap methods will be used to identify and quantitate radicals directly from the gas phase of tobacco smoke, gasoline, and diesel automobile exhaust. Although it has been shown that the principal paramagnetic species in tar is a quinone/hydroquinone complex, further studies are needed to determine how the species is produced, what chemicals in smoke are its precursor, and whether this species binds to DNA. It is hypothesized that for whole smoke, the gas phase and tar radicals have opposing effects, one initiating and one retarding radical reactions. Study emphasis will be on whether tar protects lipids from smoke-initiated autointoxication and whether tar protects α_1-proteinase inhibitor from effects of gas phase smoke.
Results to Date:
Results are not yet available.
Financial Support:
NIH (HL-25820).

0962. LOUISIANA STATE UNIVERSITY, SCHOOL OF MEDICINE, 1542 Tulane Avenue, New Orleans, Louisiana 70112.

Project Title:
Biochemistry of Lung Proteoglycans.

Principal Investigator:
Radhakrishnamurthy, B.
Objective:
To define chemistry and function of proteoglycans in normal lungs; investigate role that proteoglycans play in pathogenesis of chronic lung diseases such as emphysema.
Methods or Approach:
Proteoglycans were isolated from different tissues of bovine lung and their composition studied. The anticoagulant activity and influence of these compounds on platelet aggregation was investigated. Enzymes involved in proteoglycan catabolism were determined in bronchoalveolar lavages from smoking baboons. Emphysema was induced in rabbits by intratracheal insertion of papain, and the composition of proteoglycans in emphysematous lungs was studied. Glycosaminoglycan composition in lungs of germ-free dogs was also studied.
Results to Date:
Major proteoglycans in gas-exchange tissue and in pleura of bovine lung have been found to be heparan sulfate. These proteoglycans delayed clotting time in several assay systems and inhibited platelet aggregation. Cigarette smoking increased activities of β-N-acetylglucosaminidase, β-galactosidase, and β-glucuronidase in bronchioalveolar lavages from baboons. Protease-induced emphysema resulted in low molecular weight proteoglycans in lungs of rabbits, and concentration of glycosaminoglycans increased in emphysema.
Future Plans:
Studies will be conducted on metabolism of proteoglycans in explant cultures of lung tissues from experimental models of emphysema.
Project Dates:
December 1977–November 1983.
Financial Support:
NHLBI (2R01HL21649).

0963. LOUISIANA STATE UNIVERSITY, SCHOOL OF MEDICINE, 1542 Tulane Avenue, New Orleans, Louisiana 70112. HARBOR-UCLA MEDICAL CENTER, Torrance, California 90502.

Project Title:
Changes in Serum IgD in Cigarette Smokers.

Principal Investigators:
Bahna, S.L.; Heiner, D.C.; Myhre, B.A.
Objective:
To measure serum immunoglobulin D (IgD) levels in healthy adults; analyze data according to smoking status, degree of smoking, active inhalation of smoke, duration of smoking, and cessation of smoking.
Methods or Approach:
Serum IgD levels in 83 healthy adults were measured by radioimmunoassay and analyzed according to individual smoking habits.
Results to Date:
The IgD geometric mean in cigarette smokers was twice as high as in nonsmokers (408.6 vs. 202.0 μg/dL). Serum IgD levels of 1,000 μg/dL or greater were noted in 22 percent of smokers but in none of the occasional smokers or nonsmokers. Among smokers, the highest mean IgD level was found in those who did not actively inhale smoke (762.6 μg/dL), followed by that in moderate smokers (563.8 μg/dL). Lowest levels were found in heavy smokers who inhaled (283.0 μg/dL). In ex-smokers, mean IgD level (199.8 μg/dL) was similar to that in nonsmokers, suggesting reversibility of IgD changes following cessation of smoking. It would appear that smoking habits should be considered when interpreting serum IgD levels.
Financial Support:
NICHHD (09327).
Reference:
Bahna, S.L.; Heiner, D.C.; Myhre, B.A. "Changes in Serum IgD in Cigarette Smokers." *Clinical and Experimental Immunology* 51:624-630, 1983.

0964. TULANE UNIVERSITY, SCHOOL OF MEDICINE, 1700 Perdido Street, New Orleans, Louisiana 70112.

Project Title:
Cytotoxic Cell Function in Carcinoma of the Lung.

Principal Investigator:
DeShazo, R.D.
Objective:
To determine the effects of smoking on cytotoxic cell function and carcinogenesis.
Methods or Approach:
Cytotoxicity assays in human lung will be used.
Results to Date:
Project is in a preliminary phase.
Project Dates:
August 1984–continuing.

Financial Support:
Tulane University; VA; Cancer Association of New Orleans.

0965. TULANE UNIVERSITY, Department of Biomedical Engineering, New Orleans, Louisiana 70118.

Project Title:
Thoracic Sound Transmission.

Principal Investigators:
Rice, D.A.; Waring, W.; Beckerman, R., et al.
Objective:
To develop methods of early detection of small airway disease using audible sounds.
Methods or Approach:
Sound transmitted into the mouth and received on the thorax is changed by transmission through the lung. Studies in excised lungs indicate that transmission parameters (particularly time delay) depend on small airway characteristics. The study will test effectiveness of this approach in adult smokers and nonsmokers by comparing acoustic measurements with standard spirometric variables.
Results to Date:
Results are not yet available. Acoustic complexity (discovery of dispersion) has required new methods of signal analysis.
Project Dates:
June 1983–May 1986.
Financial Support:
NHLBI (HL 30359).

0966. TULANE UNIVERSITY, SCHOOL OF MEDICINE, 1700 Perdido Street, New Orleans, Louisiana 70112.

Project Title:
Environmental Tobacco Smoke Respiratory Disease.

Principal Investigators:
Salvaggio, J.; Lehrer, S.
Objective:
To (1) determine effects of environmental tobacco smoke on atopic and nonatopic subjects; (2) determine possible immunogenicity and allergenicity of tobacco smoke products in man; (3) examine the relationship between any putative tobacco smoke allergens and "tobacco smoke" asthma; (4) isolate and analyze immunogenic components of tobacco smoke; (5) characterize their physical and chemical properties; and (6) assay for detection of specific IgE antibody in the population against these products.
Methods or Approach:
Subjects (atopic and nonatopic individuals and smokers, ex-smokers, and nonsmokers) were selected on the basis of clinical sensitivity to tobacco smoke. Sensitive individuals were defined as those who claimed conjunctival, nasal, and/or bronchial symptoms on exposure to tobacco smoke. Nonsensitive controls (atopic and nonatopic) were age- and sex-matched volunteers. All subjects were interviewed with standard questionnaire to determine tobacco smoke sensitivity and were skin-prick tested with 16 local inhalant allergens and extracts of tobacco leaf and smoke. A small blood sample was taken for determination of antibody to tobacco leaf and smoke extracts.
Results to Date:
Of the 93 persons tested, 60 (65 percent) claimed clinical sensitivity to smoke. The majority of these individuals reported respiratory symptoms. Approximately 28 percent of the total population had positive immediate wheal and flare skin tests to at least one of the three tobacco leaf extracts tested, whereas only 12 percent had positive skin tests to one of the smoke extracts. Most individuals that had positive skin reactions were atopic. No significant differences were observed among sensitive and nonsensitive subjects with regard to skin test reactivity to tobacco leaf or smoke extracts when subjects were controlled for atopy. IgE antibody responses were detected primarily to one tobacco leaf extract. However, responses did not differ significantly in sensitive vs. nonsensitive subjects. Precipitin responses were detected to one tobacco leaf extract in approximately 40 percent of nonsensitive persons and in 61 percent of sensitive subjects; however, no relationship to smoking history or smoke sensitivity was found.
Project Dates:
1975–1983.
Financial Support:
NIAID (AI 13401).
Reference:
Lehrer, S.B.; Barbandi, F.; Taylor, J.P., et al. "Tobacco Smoke 'Sensitivity'–Is There an Immunologic Basis?" *Journal of Allergy and Clinical Immunology* 73(2):240-245, February 1984.

0967. VETERANS ADMINISTRATION MEDICAL CENTER, 1601 Perdido Street, New Orleans, Louisiana 70146.

Project Title:
The Control, Discouragement and Cessation of Smoking in a Hospital Setting.

Principal Investigator:
Dawley, H.H., Jr.
Objective:
To investigate the efficacy of cost-effective and practical programs for control, discouragement, and cessation of smoking in a hospital setting.
Methods or Approach:
Various behavioral approaches are being investigated on a continuing basis. For hospital patients, rapid smoking is not a feasible treatment because of the inherent health risks, and does not appear to be particularly effective; results fail to generalize beyond treatment. Therefore, educational approaches were designed to increase awareness of the hazards of smoking with (1) health warning signs at entrances and at point of sale of cigarettes; (2) antismoking material on wards and in waiting rooms; (3) humorous antismoking posters placed throughout the hospital; (4) daily showing of three antismoking films on closed circuit television; (5) large visual displays in the main waiting room and hallway showing the effects of smoking on the body; and (6) enforcement of existing hospital policy on smoking. The effect of differently worded "No Smoking" signs and the modeling effect of doctors smoking in the presence of patients were also investigated. The hospital participated in the American Cancer Society's Great American Smokeout Day.
Results to Date:
Findings suggest that there are practical, cost-effective environmental approaches that can be initiated to control and discourage smoking in a hospital setting. A medical center policy designating smoking and no smoking areas along with enforcement appears to be capable of reducing the smoking rate. Specifically, positively worded no smoking signs produced better compliance than negatively worded signs. Both patient and doctor smoking models significantly increased the smoking rate. Participation in the smoke-out day produced 595 pledges, with 18 percent abstinence at 2-month followup. The 6-month abstinence rate for participants in the smoking

cessation program was 53 percent of those who completed treatment.

Project Dates:
June 1974–June 1994.

Financial Support:
VA Medical Center.

References:
(1) Dawley, H.H. "To Smoke or Not: Freedom of Choice Is the Best Choice." *Respiratory Care* 25(2):230-237, 1980. (2) Dawley, H.H. "When the Smoke Clears." *APA Monitor* 11(3):3, 1983. (3) Dawley, H.H.; Morrison, J.; Carrol, S. "The Discouragement of Smoking in a Hospital Setting: The Importance of Modeled Behavior." *International Journal of Addictions* 16(5):905-910, 1981. (4) Dawley, H.H.; Morrison, J.; Carrol, S. "The Effect of Differently Worded No-Smoking Signs on Smoking Behavior." *International Journal of Addictions* 16(8):1467-1471, 1981. (5) Dawley, H.H.; Ballwin, J. "Smoking Rate in Designated Hospital Smoking and No Smoking Areas." *International Journal of Addictions* 18(7):1033-1038, 1983. (6) Dawley, H.H.; Butleer, B.; Dawley, L.T., et al. "The Discouragement of Smoking in a Hospital Setting: An Example of Worksite Smoking Discouragement." *International Journal of Addictions* (In press). (7) Dawley, H.H.; Fleischer, B.; Dawley, L.T. "Smoking Cessation With Hospital Employees: An Example of Worksite Cessation." *International Journal of Addictions* (In press). (8) Dawley, H.H.; Fleischer, B.; Dawley, L.T. "Attitudes Toward Smoking and Smoking Rate: Implications for Smoking Discouragement." *International Journal of Addictions (In press). (9) Dawley, H.H.; McKay, B. "Smoking Control in a Hospital Setting." Addictive Behaviors* (In press).

0968. VETERANS ADMINISTRATION MEDICAL CENTER, 1601 Perdido Street, New Orleans, Louisiana 70146.

Project Title:
Experimental Reduction and Elimination of Smoking Behavior by the Use of Behavioral Procedures.

Principal Investigator:
Dawley, H.H.

Objective:
To reduce and eliminate smoking through a variety of behavioral procedures.

Methods or Approach:
Initial treatment efforts dealt with using aversive smoking (rapid smoking, smoking air, and handling of cigarette litter). Attention was next directed to the study of environmental manipulations and their effect on smoking. Differently worded no-smoking signs were posted. The modeling effect on patients' smoking behavior was then assessed by having a model "patient" and "doctor" smoke in their presence in a no-smoking area. A hospitalwide smoking discouragement program was then initiated, consisting of distribution of antismoking material, humorous antismoking posters, showing of antismoking films on hospital TV system, and placement of large displays. A survey measuring patient attitudes toward smoking and a smoking cessation treatment is administered every 4 years. Efforts have also been directed at assisting hospital employees to stop smoking. Compliance to posted no-smoking areas with and without enforcement was studied. Attention is now being directed to helping hospital patients stop smoking.

Results to Date:
Twelve months after aversive smoking treatment, over 75 percent of the participants had returned to their previous rate of smoking. No-smoking signs produced an initial decrease in smoking behavior (with positively worded signs producing better compliance), followed by a return to smoking by employees first and then patients. Modeling of smoking in a no-smoking area resulted in a clear increase in the smoking rate. The hospitalwide smoking discouragement program resulted in a decrease in the male smoking rate in the main lobby smoking area and a reduction in monthly average tobacco sales while total sales increased. Results of the smoking survey over the last 8 years show that the majority of patients smoke and the majority of these smokers are interested in participating in smoking cessation efforts. Approximately 30 employees have participated in a smoking cessation program, with results of a 6-month followup being quite favorable. Enforcement of posted no-smoking areas was essential to protect patients from passive smoking.

Financial Support:
VA.

Maine

0969. FOUNDATION FOR BLOOD RESEARCH, P.O. Box 190, Scarborough, Maine 04074.

Project Title:
Cotinine Assisted Intervention to Reduce Smoking During Pregnancy.

Principal Investigators:
Haddow, J.E.; Knight, G.J.

Objective:
To test the hypothesis that it is possible to reduce or eliminate smoking in a significant percentage of pregnant women in the second trimester via a combination of serum cotinine measurements and education material (cotinine-assisted intervention); determine whether cessation or reduction of smoking starting at 16 to 20 weeks of gestation can increase mean birth weight and decrease incidence of low birth weight outcome.

Methods or Approach:
Women in the second trimester of pregnancy who enroll in an alpha-fetoprotein screening program are asked how many cigarettes are smoked/day. Those who smoke ≥ 10 cigarettes/day are randomized into intervention and nonintervention groups. In the intervention group, cotinine measurements are performed; results, along with smoking abatement information, are sent to the physician. Repeat serum cotinine measurements are offered 1 month later as an objective measure of compliance. Intervention and nonintervention groups will be compared to determine whether altered smoking behavior as measured by reduction in serum cotinine in the intervention group is reflected in increased birth weight.

Results to Date:
At the end of the first year (sixth month of intervention), 87 physicians' offices (91 percent response) were participating and 300 women were enrolled. Outcome information on subjects is being collected as births occur. Preliminary analysis of initial

and followup cotinine measurements indicate that approximately one-third of the intervention group had reduced cotinine levels by >50 percent, which is consistent with reduced smoking. The effect of this reduction will not be known until all pregnancy outcomes are documented and the relationship between outcome and cotinine reduction is analyzed.

Future Plans:
Recruitment of additional physicians will continue. It is anticipated that 3,000 women will have participated by the end of the study.

Project Dates:
February 1985–January 1989.

Financial Support:
NICHHD (1R01HD18274-02).

0970. VETERANS ADMINISTRATION, Route 17 East, Togus, Maine 04330.

Project Title:
Smoking in a Medical Center; Four Year Trends.

Principal Investigators:
Cowing, D.E.; Sattin, D.; Furbush, W.

Objective:
To identify smoking habits at the Veterans Administration Medical Center in Togus; identify nonsmokers, smokers, and ex-smokers by sex, age group, and service.

Methods or Approach:
A questionnaire formulated by the Smoking and Health Committee will be distributed to all employees at the Togus center. The data from the smoking survey questionnaire will be tabulated and evaluated.

Results to Date:
The partial results of the previous survey have been tabulated and data are available to contrast with the present survey.

Financial Support:
VA.

Maryland

0971. DHHS, NATIONAL INSTITUTE ON DRUG ABUSE, Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857.

Project Title:
Addiction Mortality in the United States, 1980: Tobacco, Alcohol, and Other Substances.

Principal Investigator:
Ravenholt, R.T.

Objective:
To determine nature and magnitude of morbidity and mortality from abuse of addictive substances.

Methods or Approach:
With the help of National Library of Medicine computers, literature on tobacco, alcohol, heroin, cocaine, and other drugs was surveyed, and titles, abstracts, and copies of recent relevant articles were obtained. A printout of U.S. mortality by every cause in 1980 was obtained from the National Center for Health Statistics to facilitate identification of drug-related deaths by discrete categories. Colleges and government agencies supplied pertinent publications and participated in work group discussions of methods and findings. Estimates were made for each substance contributing to addiction mortality to determine overall mortality.

Results to Date:
It is estimated that 147,000 of the 416,510 total cancer deaths in 1980 (35 percent) were excess cancer deaths caused by smoking cigarettes, and because cancer mortality rates not caused by smoking have continued to decrease during recent years, it is estimated that approximately 40 percent of all cancer deaths in 1984 are attributable to tobacco (smoking cigarettes, pipes, and cigars; breathing tobacco smoke generated by others; and chewing tobacco and using snuff). For cardiovascular diseases, excess mortality in 1980 due to smoking is estimated at 240,000 deaths (24 percent). Total mortality from noncancerous diseases of the respiratory system attributable to smoking was approximately 61,000 deaths. There was also excess mortality attributable to smoking for peptic ulcer disease and cirrhosis of the liver and from a broad range of miscellaneous and ill-defined diseases. Maternal smoking was an important contributor to overall infant mortality. Total excess deaths in 1980 attributable to cigarette smoking was approximately 485,000; adding those from other exposures brings the total tobacco-related mortality to probably 500,000, more than 25 percent of all deaths from all causes. Altogether, mortality in the United States during 1980 attributable to addictive substances totaled about 630,000 deaths (100,000 from alcohol and 30,000 from other addictive substances), which was nearly one-third of all deaths from all causes. The analysis clearly indicates that addiction is currently the foremost preventable cause of precocious illness and death.

Reference:
Ravenholt, R.T. "Addiction Mortality in the United States, 1980: Tobacco, Alcohol, and Other Substances." *Population and Development Review* 10(4):697-724, December 1984.

0972. DHHS, OFFICE ON SMOKING AND HEALTH, Park Building, Room 116, 5600 Fishers Lane, Rockville, Maryland 20857.

Project Title:
Feasibility Study Relating to the Validity of Responses Received From Teens About Their Smoking Status During Surveys.

Principal Investigators:
Shopland, D.R.; Lynn, W.R.

Objective:
To determine possible differences in reporting bias during surveys due to mode of interview (e.g, telephone, face-to-face) or differences between younger adolescents and older adolescents.

Methods or Approach:
Questions have been raised concerning validity of responses received from adolescents relative to smoking status resulting from administration of questionnaires during surveys. An investigation of survey literature relative to teenage smoking has been undertaken to ascertain (1) documentation of possible

underreporting among adolescents; (2) impact of mode of interview on underreporting, if any; (3) differences between age groups; and (4) changes in survey design that may correct or minimize underreporting.
Results to Date:
Preliminary results indicate that the subject has received little formal attention from the survey research community, as reflected by the scarcity of data. A number of recommendations are proposed that address the topic as a research design problem, including use of a salted sample (smoking status of subjects is known prior to interview).
Future Plans:
Recommendations from the feasibility study will be reviewed prior to conducting the sixth survey of teenage smoking prevalence in 1986.
Project Dates:
September 1984–May 1985.
Financial Support:
OSH.

0973. DHHS, OFFICE ON SMOKING AND HEALTH, Park Building, Room 116, 5600 Fishers Lane, Rockville, Maryland 20857.

Project Title:
Smoking Supplement to the September Current Population Survey.

Principal Investigators:
Shopland, D.R.; Brown, C.
Objective:
To obtain accurate State estimates of the prevalence of cigarette smoking; provide currently unavailable estimates of smoking prevalence among selected occupational groups and estimates of use of other tobacco products (snuff, chewing tobacco, pipes, and cigars).
Methods or Approach:
The national prevalence rate for smoking is approximately 30 percent, but indications are that it varies substantially among the States. Such variations have important implications on rate of outcome variables such as smoking-related morbidity and mortality. The Current Population Survey (CPS) is a monthly survey conducted in approximately 60,000 households. The Office on Smoking and Health sponsored a survey supplement (five questions) to be used in September 1985 and September 1986. The Census Bureau will ask the questions of appropriate household members (16 years of age and over). Smoking status and tobacco use data will be obtained for approximately 58,000 households (120,000 individuals).
Results to Date:
Data collection will take place in September 1985, summary tabulations will be available in April 1986, and data tapes and advance reports will be available by December 1986. Second year data will be collected in September 1986.
Future Plans:
Half of the September 1985 households will be reinterviewed in September 1986, in addition to 29,000 new households, to allow comparison and evaluation of trends in smoking prevalence and use of other tobacco products.
Project Dates:
May 1985–continuing.
Financial Support:
OSH.

0974. DHHS, OFFICE ON SMOKING AND HEALTH, Park Building, Room 116, 5600 Fishers Lane, Rockville, Maryland 20857.

Project Title:
National Probability Survey of Adult Cigarette Smoking Prevalence, Knowledge, Attitudes, and Beliefs.

Principal Investigators:
Shopland, D.R.; Lynn, W.R.
Objective:
To ascertain present smoking behavior, knowledge, attitudes, and beliefs among adults in the United States; evaluate possible changes that have taken place since a similar survey in 1975.
Methods or Approach:
Approximately 12,000 telephone interviews are being conducted to obtain (1) current statistical data on prevalence rates of tobacco use, particularly cigarettes; (2) demographic data on smokers and nonsmokers; (3) attitudinal data on smokers and nonsmokers; (4) smoking history and consumption; (5) cigar, pipe, snuff, and chewing tobacco use; (6) knowledge and beliefs about health risks; and (7) smoking cessation. Random digit dialing, using a variation of the Waxberg method, is being used for this national probability sample. Ever smokers will be oversampled so that they comprise 75 percent of the sample. One eligible person (18 years or older) from each household will be selected for the interview. Information will be collected by a computer-assisted telephone interview system (CATI).
Results to Date:
Project is in a preliminary phase.
Project Dates:
September 1984–March 1986.
Financial Support:
OSH (282-84-0062).

0975. DHHS, PHS, ADAMHA, National Institute on Drug Abuse, Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857.

Project Title:
Tobacco Addiction and Tobacco Mortality.

Principal Investigators:
Pollin, W.; Ravenholt, R.T.
Objective:
To encourage physicians to routinely ascertain the lifetime smoking experience of each patient and state on each death certificate the role of tobacco.
Methods or Approach:
The current revision of the *International Classification of Diseases* and the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* recognize the addictive nature of smoking and provide a specific category for diseases and deaths caused by "tobacco dependence." Stipulated criteria for making a diagnosis of tobacco dependence in a patient currently undergoing treatment or dying are summarized as continuous use of tobacco for at least a month with either (1) unsuccessful attempts to stop or significantly reduce amount of tobacco used on a permanent basis, (2) development of tobacco withdrawal, or (3) presence of a serious physical disorder (e.g., respiratory or cardiovascular disease) that the individual (or physician) knows is exacerbated by tobacco use. If the individual with a serious case of one of the tobacco-related physical disorders continues to use tobacco, despite awareness of its harmful effects, a reasonable inference can be made that the individual is tobacco dependent.
Results to Date:
By routinely ascertaining lifetime smoking experience of each

patient and stating on each death certificate the role of tobacco, physicians can contribute substantially to improvement of vital statistics, epidemiology, and public health. Addictive disorders now cause more than 25 percent of all deaths in the United States; however, this fact is obscured in vital records and statistics by the general practice of certifying addictive disease deaths to innumerable manifestations.
Financial Support:
NIDA.
Reference:
Pollin, W.; Ravenholt, R.T. "Tobacco Addiction and Tobacco Mortality. Implications for Death Certification." *Journal of the American Medical Association* 252(2):2849-2854, November 23, 1984.

0976. DHHS, NATIONAL CENTER FOR HEALTH STATISTICS, 3700 East-West Highway, Hyattsville, Maryland 20782.

Project Title:
National Health and Nutrition Examination Survey I - Epidemiologic Followup Study.

Principal Investigator:
Kleinman, J.C.
Objective:
To determine current health status and inpatient health care of all persons 25 years of age and over who were participants in NHANES I (1971-1975).
Methods or Approach:
Subjects were reinterviewed after approximately 10 years by household interviews. NHANES I included data on smoking. Data were collected on current cigarette smoking, age of smoking initiation, periods of quitting for more than a year, and current use of cigars and pipes. Respondents will continue to be interviewed periodically. All respondents will be tracked against the National Death Index to determine cause of death.
Results to Date:
Results are not yet available.
Future Plans:
Research papers will be prepared; public use tapes will be available.
Project Dates:
October 1982–continuing.
Financial Support:
NCHS, NIH (NIA, NCI, NHLBI, NIADDK, NINCDS); NIMH; NIAAA.

0977. DHHS, NATIONAL CENTER FOR HEALTH STATISTICS, 3700 East-West Highway, Hyattsville, Maryland 20782.

Project Title:
National Natality and Fetal Mortality Followback Survey (1980).

Principal Investigator:
Placek, P.
Objective:
To collect birth-related data not usually available on vital records, including smoking status and alcohol use before and during pregnancy, prenatal care, and sociodemographic characteristics of mother and father.
Methods or Approach:
Data were collected by mail questionnaire from parents of about 10,000 live births and 6,500 fetal deaths. Data were also obtained from physicians and hospitals.
Results to Date:
Data have been published; public use tapes are available.
Future Plans:
Survey will be repeated in 1988.
Project Dates:
1980–continuing.
Financial Support:
NCHS, FDA, NIH (NICHD), HRSA, NIAAA, NIDA, CDC, NIOSH.
Reference:
Prager, K.; Malin, H.; Spiegler, D., et al. "Smoking and Drinking Behavior Before and During Pregnancy of Married Mothers of Live-Born Infants and Stillborn Infants." *Public Health Reports* 99(2):117-127, March-April 1984.

0978. DHHS, NATIONAL CENTER FOR HEALTH STATISTICS, 3700 East-West Highway, Hyattsville, Maryland 20782.

Project Title:
Hispanic Health and Nutrition Examination Survey (HHANES) 1982-84.

Principal Investigator:
Murphy, R.
Objective:
To collect data on cigarette, cigar, and pipe smoking among the U.S. Hispanic population.
Methods or Approach:
Data are obtained on age started smoking cigarettes, heaviest amount and current amount smoked, brand name (for tar/nicotine levels), and age at quitting for former smokers. Only current amount smoked is collected for cigars and pipes. Data can be related to all the health examination, clinical, and laboratory information obtained on HHANES. Probability samples of Mexican-Americans in the Southwest, Cuban-Americans in Florida, and Puerto Ricans in New York City were interviewed and given extensive physical examinations in mobile clinics. Smoking data were obtained on about 13,000 persons between the ages of 12 and 74.
Results to Date:
Results are not yet available.
Future Plans:
Data will be published in NCHS reports and will be available on public use data tapes.
Project Dates:
July 1982–December 1984.
Financial Support:
NCHS; NIH (NHLBI, NIADDK, NICHD, NIDR, NINCDS); ADAMHA; FDA; EPA; USDA.

0979. DHHS, NATIONAL CENTER FOR HEALTH STATISTICS, 3700 East-West Highway, Hyattsville, Maryland 20782.

Project Title:
National Health Interview Survey (NHIS) 1983 Alcohol/Health Practices Supplement.

Principal Investigator:
Fuchsberg, R.R.
Objective:
To collect data on cigarette smoking by adults (civilian noninstitutional population) in the United States.
Methods or Approach:
Data were obtained on current cigarette smoking status, number of cigarettes smoked, quitting date for former smokers, and cessation methods attempted in past 5 years. Results can

be related to all health data collected by NHIS. Household interviews, conducted by Bureau of the Census interviewers, sampled approximately 25,000 adults 18 years of age and older.

Results to Date:
Provisional results have been published. Data are shown by sex and age for 1965, 1970, 1976, 1980, and 1983, and indicate percent of current and former smokers and amount smoked (< 15/day, 15 to 24/day, and ≥ 25/day). Data on earlier years are also shown by race.

Future Plans:
Additional reports will be published and public use data tapes will be available.

Project Dates:
January 1983–January 1984.

Financial Support:
NCHS; NIAAA.

0980. DHHS, NATIONAL CENTER FOR HEALTH STATISTICS, 3700 East-West Highway, Hyattsville, Maryland 20782.

Project Title:
National Health Interview Survey (NHIS) 1985 Promotion Supplement.

Principal Investigator:
Fuchsberg, R.R.

Objective:
To collect information to track 1990 health promotion objectives.

Methods or Approach:
Data are collected on cigarette smoking and pregnancy, current smoking, amount smoked, and knowledge of risk factors associated with cigarette smoking. Data can be related to other health behaviors and other health data on the NHIS. Household interviews, conducted by Bureau of the Census interviewers, sampled approximately 35,000 adults 18 years of age and older. The survey will be repeated in 1990.

Results to Date:
Provisional estimates will be available in late 1985.

Future Plans:
Data to be published in NCHS reports and public use data tapes will be available.

Project Dates:
January 1985–January 1986.

Financial Support:
NCHS; HRSA; CDC; NIOSH; NIH (NHLBI, NIDR); NIAAA; OASH (ODPHP).

0981. DHHS, NATIONAL CENTER FOR HEALTH STATISTICS, 3700 East-West Highway, Hyattsville, Maryland 20782.

Project Title:
National Survey of Family Growth.

Principal Investigator:
Pratt, W.

Objective:
To collect data on a wide range of variables related to dynamics of population change, family planning, and maternal and child health, including cigarette smoking during pregnancy.

Methods or Approach:
Data were obtained in household interviews of about 8,000 women between the ages of 15 and 44.

Results to Date:
Results are not yet available.

Future Plans:
NCHS reports and public use tapes will be available.

Project Dates:
September 1982–February 1983.

Financial Support:
NCHS; NIH (NICHD); OASH (OAPP).

0982. DHHS, NIH, NATIONAL CANCER INSTITUTE, 9000 Wisconsin Avenue, Building 37, Room 2C09, Bethesda, Maryland 20205.

Project Title:
Detection of Benzo(*a*)pyrene Diol Epoxide Adducts in Peripheral Blood Lymphocytes and Antibodies to the Adducts in Sera From Individuals With High Cancer Risk Exposure.

Principal Investigators:
Harris, C.C.; Vahakangas, K.; Newman, M.J., et al.

Objective:
To develop assays and field study protocols that will allow qualitative and quantitative determination of individuals at risk for development of lung cancer due to exposure to major carcinogens that cause cancer in animals and are prevalent in human social and occupational environments.

Methods or Approach:
Benzo(*c*)pyrene diolepoxide (BPDE) forms adducts with animal and human DNA. Peripheral whole blood is drawn from smokers and nonsmokers among highly exposed workers, cancer patients, or normal volunteers and separated into erythrocytes, leukocytes, and serum or plasma. Phenol-extracted DNA from the leukocytes is assayed for BPDE adducts and sera are tested for anti-BPDE antibodies. DNA is examined by (1) ultrasensitive radioimmunoassay (USERIA), an immunoassay using anti-BPDE-DNA antibodies and radiolabeled enzyme substrates, and (2) synchronous fluorescence spectrophotometry (SFS), which detects the highly fluorescent nuclei of BPDE-tetrols. Both detect < 1 mol BaP in 10^7 mol nucleotides. Antibodies to BPDE are detected with a modified ELISA using in vitro modified BPDE-DNA as the target antigen. Bronchial washings and alveolar macrophages of lung cancer patients and smokers are also being investigated.

Results to Date:
BPDE-DNA adducts were detected in 25 percent of roofers and in 35 to 65 percent of coke oven workers from three plants (total, 50 of 102 smoking and nonsmoking coke oven workers and 7 of 28 roofers). In addition, 11 of 44 coke oven workers from one plant had detectable antibodies to BPDE-DNA, and only 2 cases (of 4 with highest titers) had no detectable adducts. In general, smokers had higher incidences and larger amounts of detectable adducts. USERIA and SFS agreed consistently in cases with highest detectable adducts. At lower adduct levels, USERIA was more effective, owing largely to some practical differences in methodology currently being studied. Approximately 25 unexposed cases were negative for both adducts and antibodies.

Future Plans:
Testing of exposed and unexposed smokers and nonsmokers will continue, to achieve statistical expansion of preliminary results; cases with continuing exposure and those with discontinued exposure will be tested repeatedly to study persistence, appearance, or fluctuation of BPDE-DNA adducts and antibody positivity in human populations. The relationship of these phenomena to related diseases will be observed.

Project Dates:
May 1979–continuing.

Financial Support:
NCI.

0983. DHHS, NIH, ADAMHA, NATIONAL INSTITUTE OF MENTAL HEALTH, Biological Psychiatry Branch, Building 10, Room 3N212, Bethesda, Maryland 20205.

Project Title:
Location and Function of Central Nicotinic Receptors.

Principal Investigators:
Clarke, P.B.S.; Pert, A.
Objective:
To (1) localize putative central receptors for acetylcholine and nicotine; (2) compare data obtained from autoradiographic nicotinic binding studies with functional measures of nicotine's central actions; and (3) develop selective central antagonists of nicotine.
Methods or Approach:
Research will include (1) autoradiographic mapping of high-affinity binding of acetylcholine, nicotine, and α-bungarotoxin to brain sections; neurochemical and surgical lesions to identify neuronal locus of binding; (2) response of identified brainstem neurons to systemically or microiontophoretically applied nicotinic agents in rats; and (3) microinjection of drugs and into brain sites to localize locomotor stimulant action of nicotine in rats.
Results to Date:
Two neuroanatomically distinct populations of brain nicotine receptors, differentially labeled with tritiated nicotine (or acetylcholine) and iodinated α-bungarotoxin, were identified. Dopamine neurons of the substantia nigra possess tritiated nicotine binding sites and are stimulated by systemic or direct application of nicotine. Nicotine receptors are differentially distributed within the interpeduncular nucleus and are partly located on presynaptic afferents, presumably cholinergic. Experiments in rats suggest possible therapeutic use of a long-acting central nicotinic antagonist.
Future Plans:
Research will concentrate on (1) distribution of nicotine receptors in primates; (2) functional identification of a putative cholinergic termination in substantia nigra; and (3) interactions between acetylcholine and other neurotransmitters assessed electrophysiologically.
Project Dates:
November 1982–November 1985.
Financial Support:
NIMH.

0984. DHHS, NIH, NATIONAL CANCER INSTITUTE, LABORATORY OF CELLULAR CARCINOGENESIS AND TUMOR PROMOTION, National Institutes of Health, Bethesda, Maryland 20205.

Project Title:
Use of Immunological Techniques to Study Interaction of Carcinogens With DNA.

Principal Investigators:
Poirier, M.C.; Yuspa, S.H.; Reed, E., et al.
Objective:
To probe, with antibodies specific for carcinogen-DNA adducts, the nature, extent, and consequences of in vitro and in vivo DNA modification.
Methods or Approach:
Biological samples of DNA substituted with 2-acetylaminofluorene (AAF), benzo(*a*)pyrene (BaP), or cis-dichlorodiammineplatinum (II) (cis-DDP) were subjected to immunological localization and quantitative immunoassays able to detect 1 adduct in 100 million nucleotides.
Results to Date:
In hepatic DNA of rats fed a carcinogenic level of AAF for 4 weeks, adduct accumulation reached a plateau at 2 to 3 weeks. During 4 weeks on a control diet, adduct removal was biphasic, with a rapid initial phase followed by a slow second phase. A pharmacokinetic model consistent with this data proposes that adducts are formed in two DNA compartments, one from which adducts are removed rapidly and another from which adducts are removed slowly. Persistent adducts accumulate in the slow-repairing compartment, but constitute less than 7 percent of the total adducts formed. In contrast to the high levels of AAF adducts in liver DNA, binding of BaP to deoxyguanosine (dG) in DNA of mouse epidermis and cultured epidermal cells was more than fifty-fold lower. Binding levels were similar in epidermis and epidermal cells, subsequent to dosages known to induce papillomas in vivo and differentiation-altered foci in the cultured feratinocytes. The kinetics of repair for BaPdG in vivo and in vitro were biphasic (as in liver), but much more rapid, with 50 percent removal by 1 to 2 days. Thus, adduct accumulation and removal seem to be characteristic of interaction between a particular target tissue and an individual carcinogen, and may not be quantitatively related to efficiency of tumorigenesis or transformation. Antisera specific for cis-DDP-DNA have been used to measure adducts in DNA of nucleated blood cells from cancer patients on platinum drug chemotherapy. Adducts appear to accumulate both as a function of total cumulative dose and of increasing cycle number in individuals who have not received previous platinum drug therapy. The relationship between ability to form adducts and disease response appears promising.
Project Dates:
October 1983–September 1984.
Financial Support:
NCI (Z01CP05177-03 CCTP).

0985. DHHS, NIH, NATIONAL CANCER INSTITUTE, Blair Building, National Institutes of Health, Bethesda, Maryland 20205.

Project Title:
Dark Tobacco and Lung Cancer in Cuba.

Principal Investigators:
Joly, O.G.; Lubin, J.H.; Caraballoso, M.
Objective:
To determine whether the high lung cancer mortality rates in Cuba can be explained by cigarette and cigar smoking habits, including the smoking of dark tobacco cigarettes.
Methods or Approach:
A retrospective epidemiologic study was conducted of 826 cytologically and/or histologically confirmed lung cancer cases (219 females, 607 males), 979 hospital controls, and 539 neighborhood controls in Havana, Cuba.
Results to Date:
Relative risk (RR) of lung cancer among cigarette smokers was 7.3 in women and 14.1 in men and increased consistently with various measures of exposure to smoke. Findings suggest that duration of smoking, number of cigarettes smoked/day, and inhalation practices have independent effects. Most Cubans smoke dark tobacco, and RR was higher for dark tobacco users than for light tobacco users; 8.8 vs. 4.6 for women and 14.3 vs. 11.3 for men, respectively. However, differences were reduced after adjustment for amount smoked. Cigarette smoking was associated with all histologic types of lung cancer, although the risk for adenocarcinoma was lower than for other types. Men who smoked cigars exclusively had a fourfold risk of lung

cancer, while smokers of both cigarettes and cigars had a greater RR than cigarette-only smokers (15.0 vs. 14.1), perhaps related to the unusually deep and frequent inhalation of cigar smoke. Data support the hypothesis that smoking patterns account for the higher lung cancer mortality in Cuba than in other Latin American countries.

Financial Support:
NCI.

Reference:
Joly, O.G.; Lubin, J.H.; Caraballoso, M. "Dark Tobacco and Lung Cancer in Cuba." *Journal of the National Cancer Institute* 70(6):1033-1039, June 1983.

0986. DHHS, NIH, NATIONAL CANCER INSTITUTE, Blair Building, Room 6A09, Bethesda, Maryland 20205. NATIONAL PUBLIC HEALTH INSTITUTE, Mannerheimintie 166, SF-00280, Helsinki 28, Finland.

Project Title:
U.S.–Finland Studies of Nutrition and Cancer.

Principal Investigators:
Heinonen, O.P.; Huttunen, J.K.; Albanes, D.

Objective:
To evaluate effectiveness of beta-carotene and/or alpha-tocopherol (vitamin E) dietary supplementation in preventing lung cancer in high-risk smoking males; study effect of these factors on occurrence of cancer at other sites.

Methods or Approach:
The United States–Finland Studies of Nutrition and Cancer is a project consisting of three studies conducted in Finland through the National Public Health Institute. Two of the three studies are (1) a breast cancer case–control study of dietary and serum nutrient factors; and (2) a dietary survey cohort study. However, primary emphasis is a beta-carotene, alpha-tocopherol lung cancer prevention trial, which will test the efficacy of daily oral administration of 20 mg beta-carotene and/or 50 mg vitamin E for prevention of lung cancer. Approximately 18,000 males aged 50 to 69 who currently smoke five or more cigarettes/day will be blindly randomized to one of four intervention groups: beta-carotene alone; vitamin E alone; both agents; or placebo. Intervention will be for 5 years for each subject. Changes in smoking habit and dietary and pill compliance will be monitored throughout. Incident lung cancer cases (and cancers of other sites) will serve as primary trial endpoints.

Results to Date:
A pilot phase of the clinical trial will be completed in April 1985 for 500 participants.

Future Plans:
The lung cancer prevention trial will include five clinics, beginning in April 1985. Ancillary studies in areas of dietary methodology, subject compliance, toxicity monitoring, and serum nutrient analysis will also be conducted.

Project Dates:
March 1984–February 1992.

Financial Support:
NCI (N01CN45165).

0987. DHHS, PHS, NIH, NATIONAL HEART, LUNG AND BLOOD INSTITUTE, Division of Heart and Vascular Diseases, Bethesda, Maryland 20205.

Project Title:
Framingham Heart Study.

Principal Investigators:
Castelli, W.P.; Kannel, W.B.; Stokes, J., III, et al.

Objective:
To investigate all factors related to the development of coronary heart disease (CHD), stroke, and other medical (cancer) endpoints.

Methods or Approach:
Among women who were aged 30 to 49 at the first Framingham Heart Study biennial examination in 1949, 45 percent reported smoking cigarettes. Development of clinically recognizable myocardial infarction (MI) was determined on each biennial examination over 26 years. The women received an examination that included medical history, examination of the cardiovascular system, electrocardiogram, lung function test, and blood analyses. Studies of the lipoprotein cholesterol profiles were carried out at biennial examination 11.

Results to Date:
Women who reported smoking cigarettes at the first examination were about twice as likely to develop MI as were nonsmoking women. When adjustments for changes in smoking habits were taken into account by examining "accumulated" 8-year incidence, the relationship between cigarette smoking and MI was even more pronounced. The lipoprotein cholesterol profile tests revealed higher LDL and VLDL cholesterol and lower HDL cholesterol in women who smoke. These differences are in the same direction as men but of larger magnitude. This suggests that at least a portion of the CHD morbidity associated with cigarette smoking may result from enhanced atherogenesis secondary to altered lipoprotein cholesterol patterns. The results also demonstrate an elevated long-term risk of clinically severe CHD in those who smoke cigarettes, and confirm similar findings that have been apparent since early in the study for men in the Framingham Heart Study.

Future Plans:
In addition to continued surveillance for MI, women have been tested for the presence of ventricular arrhythmias by 1-hour ambulatory ECG monitoring at biennial examinations. How lifetime cigarette history relates to the occurrence of symptoms of cardiac dysfunction will be investigated.

Project Dates:
1949–continuing.

Financial Support:
NHLBI.

0988. DHHS, PHS, NIH, NATIONAL CANCER INSTITUTE, 7910 Woodmont Avenue, Bethesda, Maryland 20205.

Project Title:
Epidemiologic Studies of Tobacco Use and the Risk of Cancer.

Principal Investigators:
Blot, W.J.; Brown, L.M.; Ershow, A., et al.

Objective:
To examine the relationship between the use of tobacco, particularly snuff, chewing tobacco, and cigarettes, in the risk of cancer in human populations; examine interactions between tobacco use and environmental and occupational determinants of cancer occurrence in human populations.

Methods or Approach:
The methods and approaches include case–control studies of specific cancers, usually involving personal interviews using structured questionnaires, analysis of cohort studies of population groups with known tobacco habits, and descriptive and ecologic studies using national and local vital records and demographic data.

Results to Date:

A series of case–control studies revealed that tobacco consumption contributes to the high risk of cancer in certain areas of the United States. The long-term oral use of snuff was shown to account for the sharply elevated mortality from oral cancer among women in the South. Smoking was linked to the high rate of esophageal cancer among black males in Washington D.C., where esophageal mortality rates are highest in the country, although alcohol consumption was the dominant risk factor. Smoking appeared to enhance the risk of lung cancer among shipyard workers, accounting in part for excess rates of this cancer in control areas of the country; in contrast, no positive association between smoking and mesothelioma was observed in coastal Virginia where this cancer occurs with elevated frequency. Cigarette smoking was shown to be the primary determinant of increased risk of cancer of the renal pelvis, and to significantly contribute to renal adenocarcinoma in a study in high risk areas in Minnesota. Data from a large case–control study of lung cancer in western Europe showed significantly increased risks of all cell types of lung cancer, including adenocarcinoma, associated in a dose-related manner with smoking. Increased risks were also documented for persons who smoked only pipes or cigars, and the risk in smokers of filtered vs. nonfiltered cigarettes was quantified taking into account differences in intensity and duration of smoking. In Hiroshima and Nagasaki, Japan, smoking and atomic irradiation were shown to combine in an additive fashion to increase lung cancer risk.

Future Plans:

Research will continue to be conducted in high-risk areas where opportunities exist to evaluate environmental determinants, including tobacco, in cancer.

Project Dates:

1975–continuing.

Financial Support:

NCI.

References:

(1) Blot, W.J.; Davies, J.E.; Brown, L.M., et al. "Occupation and the High Risk of Lung Cancer in Northeast Florida." *Cancer* pp. 364-371, 1982. (2) Blot, W.J.; Morris, L.E.; Stroube, R., et al. "Lung and Laryngeal Cancers in Relation to Shipyard Employment in Coastal Virginia." *Journal of the National Cancer Institute* 65:571-575, 1980. (3) Pottern, L.M.; Morris, L.E.; Blot, W.J., et al. "Esophageal Cancer Among Black Men in Washington, D.C. I. Alcohol, Tobacco, and Other Risk Factors." *Journal of the National Cancer Institute* 67:777-783, 1981. (4) Tagnon, I.; Blot, W.J.; Stroube, R.B., et al. "Mesothelioma Associated With the Shipbuilding Industry in Coastal Virginia." *Cancer Research* 40:3875-3879, 1980. (5) Winn, D.M.,; Blot, W.J.; Shy, C.M., et al. "Snuff Dipping and Oral Cancer Among Women in the Southern United States." *New England Journal of Medicine* 304:745-749, 1981.

0989. DHHS, PHS, NIH, NATIONAL CANCER INSTITUTE, 9000 Rockville Pike, Bethesda, Maryland 20205.

Project Title:

Field Studies in High-Risk Areas.

Principal Investigators:

Blot, W.J.; Fraumeni, J.F., Jr.; Hoover, R., et al.

Objective:

To identify and describe environmental and host determinants of cancer in areas of the United States at high risk of cancer through the use of analytical epidemiologic techniques, particularly case–control studies of specific cancers.

Methods or Approach:

Field studies are conducted in areas of the country where cancer rates are high and etiologic hypotheses can be tested. The studies are generally case–control investigations whereby cancer patients and controls, or their next of kin in the event they had died, are interviewed regarding lifetime histories of residence, occupation, tobacco consumption, diet, and medical or other factors. Comparison of responses between the cases and controls are then made by analytical epidemiologic techniques to identify, estimate, and evaluate cancer risk factors. When a particular suspect environmental or occupational exposure among a well-defined population group is recognized, cohort investigations may be initiated to determine the group's cancer experience. Often both the case–control interview and the cohort studies are preceded by reviews of appropriate death certificates and medical records for cancer cases and controls for comparisons of available information.

Results to Date:

Interview studies have been completed on (1) kidney cancer in Minnesota, showing that ethnic factors contributed to high rates in the area, but cigarette smoking and, among women, high weight-for-height were major risk factors for renal adenocarcinoma, while smoking was the predominant cause of renal pelvis cancer; (2) lung cancer in an industrialized area of eastern Pennsylvania, where an 80 percent increased risk of this cancer was found among long-term steel workers after adjusting for smoking; (3) nasal cancer in Virginia and North Carolina, showing increased risks of adenocarcinoma among furniture makers and for the first time a link between cigarette smoking and squamous cell nasal cancers; (4) lung cancer in Jacksonville, Florida, which found that increased risks associated with employment in the shipbuilding, construction, and lumber forestry industries contributed to this area being ranked first among all urban counties in the country in lung cancer mortality among white males; (5) oral cancer among women in North Carolina, showing that chronic oral snuff use is responsible for the high rates of this tumor in the southeast; and (6) esophageal cancer among black men in Washington, D.C., revealing increased rates with heavy alcohol consumption and with smoking and decreased nutritional status. Field investigations were also underway of lung, pancreas, and stomach cancer in Louisiana; respiratory cancer in Texas; and bladder cancer in rural New England.

Future Plans:

Field studies in areas where cancer rates are high will continue. Analysis of information collected in Louisiana, Texas, and rural New England will be completed. Results from these ongoing studies will help suggest where further epidemiologic research will be worthwhile.

Project Dates:

October 1980–continuing.

Financial Support:

NCI ((Z)L CP 04779-05 EEB).

References:

(1) Blair, A.; White, D.W. "Death Certificate Study of Leukemia Among Farmers From Wisconsin." *Journal of the National Cancer Institute* 66(6):1027-1081, 1981. (2) Blot, W.J.; Brown, L.M.; Pottern, L.M., et al. "Lung Cancer Among Long-Term Steel Workers." *American Journal of Epidemiology* 117:706-716, 1983. (3) Blot, W.J.; Davies, J.E.; Morris, L.E., et al. "Occupation and the High Risk of Lung Cancer in Northeast Florida." *Cancer* 50:364-371, 1982. (4) Blot, W.J.; Fraumeni, J.F., Jr. "Geographic Patterns of Cancer in the United States." In: Marks, P. (Editor). *Cancer Research in the People's Republic of China and the United States of America.* New York, Grune and Stratton, 1980, pp. 65-77. (5) Blot, W.J.; Fraumeni, J.F., Jr. "Cancer Among Shipyard Workers."

In: *Banbury Report 9: Quantification of Occupational Cancer.* Cold Spring Harbor, New York, Cold Spring Harbor Laboratory (In press). (6) Blot, W.J.; Morris, L.E.; Stroube, R., et al. "Lung and Laryngeal Cancers in Relation to Shipyard Employment in Coastal Virginia." *Journal of the National Cancer Institute* 65:571-575, 1980. (7) Brinton, L.A.; Blot, W.J.; Becker, J.A., et al. "A Case-Control Study of Cancers of the Nasal Cavity and Paranasal Sinuses." *American Journal of Epidemiology* 119:896-906, 1984. (8) Brown, L.M.; Pottern, L.M.; Blot, W.J. "Lung Cancer in Relation to Environmental Pollutants Emitted From Industrial Sources." *Environmental Research* 34:250-261, 1984. (9) Gottlieb, M.S.; Pickle, L.W. "Bladder Cancer Mortality in Louisiana." *Journal of the Louisiana State Medical Society* 133:6-9, 1981. (10) Lanier, A.P.; Blot, W.J.; Fraumeni, J.F., Jr., et al. "Cancer in Alaskan Indians, Eskimos, and Aleuts." *Journal of the National Cancer Institute* 65:1157-1159, 1980. (11) Lubin, J.H.; Blot, W.J.; Burns, P.E., et al. "Dietary Factors and Breast Cancer Risk." *International Journal of Cancer* (In press). (12) Lubin, J.H.; Burns, P.E.; Blot, W.J., et al. "Risk Factors for Breast Cancer in Northern Alberta as Related to Age at Diagnosis." *Journal of the National Cancer Institute* 68(2):211-218, 1982. (13) Mason, T.J.; Pickle, L.W. "Etiologic Study of Respiratory Cancer in Coastal Texas." In: *Proceedings of the First NCI/EPA/NIOSH Collaborative Workshop: Progress on Joint Environmental and Occupational Cancer Studies,* Rockville, Maryland, May 6-8, 1980. Washington, D.C., U.S. Government Printing Office, 1981, pp. 88-93. (14) McLaughlin, J.K.; Blot, W.J.; Mandel, J.S., et al. "Etiology of Cancer of the Renal Pelvis." *Journal of the National Cancer Institute* 71:287-291, 1983. (15) McLaughlin, J.K.; Mandel, J.S.; Blot, W.J., et al. "A Population-Based Case-Control Study of Renal Cell Carcinoma." *Journal of the National Cancer Institute* 72:275-284, 1984. (16) Pickle, L.W. "Cancer in Southern Louisiana: Progress Report of a Case-Control Study of Lung, Stomach, and Pancreas Cancer." In: *Proceedings of the First NCI/EPA/NIOSH Collaborative Workshop: Progress on Joint Environmental and Occupational Cancer Studies,* Rockville, Maryland, May 6-8, 1980. Washington, D.C., U.S. Government Printing Office, 1981, pp. 53-54. (17) Pottern, L.M.; Blot, W.J.; Fraumeni, J.F., Jr. "A Case-Control Study of Lung Cancer Near a Zinc Smelter." In: *Proceedings of the First NCI/EPA/NIOSH Collaborative Workshop: Progress on Joint Environmental and Occupational Cancer Studies,* Rockville, Maryland, May 6-8, 1980. Washington, D.C., U.S. Government Printing Office, 1981, pp. 56-62. (18) Pottern, L.M.; Morris, L.E.; Blot, W.J., et al. "Esophageal Cancer Among Black Men in Washington, D.C.-I. Alcohol, Tobacco, and Other Risk Factors." *Journal of the National Cancer Institute* 67(4):777-783, 1981. (19) Pottern, L.M.; Stone, B.J.; Day, N.E., et al. "Thyroid Cancer in Connecticut 1935-1975: An Analysis by Cell Type." *American Journal of Epidemiology* 112:764-774, 1980. (20) Tagnon, I.; Blot, W.J.; Stroube, R.B., et al. "Shipbuilding-Associated Mesothelioma in Coastal Virginia." *Cancer Research* 40:3875-3879, 1980. (21) Winn, D.M.; Blot, W.J.; Shy, C.M., et al. "Snuff Dipping and Oral Cancer Among Women in the Southern United States." *New England Journal of Medicine* 304:745-749, 1981. (22) Winn, D.M.; Ziegler, R.G.; Pickle, L.W., et al. "Diet in the Etiology of Oral and Pharyngeal Cancer Among Women From the Southern U.S." *Cancer Research* 44:1216-1222, 1984. (23) Ziegler, R.G.; Blot, W.J.; Hoover, R., et al. "Nutritional Factors and Low Risk of Colon Cancer in Southern Retirement Areas: A Study Protocol." *Cancer Research* (In press). (24) Ziegler, R.G.; Morris, L.E.; Blot, W.J., et al. "Esophageal Cancer Among Black Men in Washington, D.C.-II. The Role of Nutrition." *Journal of the National Cancer Institute* 67(6):1199-1206, 1981.

0990. DHHS, PHS, NIH, NATIONAL CANCER INSTITUTE, Laboratory of Molecular Carcinogenesis, Building 37, 3D25, Bethesda, Maryland 20205.

Project Title:

Monoclonal Antibody-Directed Phenotyping, Radioimmunoassay and Immunopurification of Cytochrome P-450 in Animal and Human Tissues.

Principal Investigators:

Park, S.S.; Fujino, T.; Song, B.J., et al.

Objective:

To identify and phenotype cytochrome P-450 as a primary step in determining the metabolic potential responsible for differences between tissues, organs, individuals, and species in sensitivity to drugs and chemical carcinogens.

Methods or Approach:

Monoclonal antibodies (MAbs) to each form of cytochrome P-450 were made. Myeloma cells and spleen cells primed with the specific isozyme were fused using polyethyleneglycol. Hybrid cells were selected in HAT medium, and MAb-producing hybrid cells were screened by radioimmunoassay (RIA). The effect of MAbs on enzyme activity was measured for aryl hydrocarbon hydroxylase (AHH) and ethoxycoumarin deethylase (ECD). Competitive RIA was done with microsomes that were used in coating microtiter wells and for competing antigens. MAb-directed immunopurification of cytochrome P-450 was done with MAb-conjugated Sepharose-4B. The degree of binding in RIA and inhibition on their enzyme activities by MAbs should quantitatively assess the contribution of a specific form of cytochrome P-450 that the MAbs recognized.

Results to Date:

AHH and ECD activities of human placentas from individual women who smoked were inhibited by 83 to 90 percent and 34 to 74 percent, respectively, by MAbs to MC-P-450. There were extraordinarily high intrapair concordance (monozygotic dichorionic twins or dizygotes) for both absolute amounts of AHH and ECD and inhibitions by MAbs compared with unrelated individuals among twin births. AHH and ECD activities in benzo(*a*)anthracene (BA)-induced lymphocytes were also inhibited by 16 to 65 percent and 30 to 78 percent, respectively. Both AAH and ECD activities in control, BA-induced monocytes and in normal liver were largely unaffected by MAbs. In RIA, microsomal preparations of human smoker's placenta and BA-induced lymphocyte homogenates also competitively inhibited binding of MAbs to methylcholanthrene (MC)-induced rat microsomes. MAbs conjugated to Sepharose-4B also selectively bind to P-450 from the mixture of microsomal proteins, and the P-450 were purified by acid cleavage from Sepharose-4B-MAbs-P-450 complexes. Results indicate that the cytochrome P-450 that is inducible by 3MC in rats is also the form inducible in human cell lines in vitro by BA and in vivo in humans by smoking.

Future Plans:

The ultimate goal will be to make monoclonal antibodies to cytochrome P-450 from animal and human sources and characterize human cytochrome P-450 to understand the differences in drug and carcinogen metabolism.

Project Dates:

February 1979–continuing.

Financial Support:

NCI.

0991. FRANCES SCOTT KEY MEDICAL CENTER, NIDA ADDICTION RESEARCH CENTER, 4940 Eastern Avenue, Baltimore, Maryland 21224.

Project Title:
Evaluation of a Drug Interview Schedule.

Principal Investigators:
Haertzen, C.A.; Haynes, A.; Hickey, J.
Objective:
To determine strength of drug habits and/or abuse of a variety of drugs including cigarettes, coffee, alcohol, valium, marijuana, heroin, LSD, PCP, glue, cocaine, specific opiates, barbiturates, stimulants, minor tranquilizers, and major tranquilizers.
Methods or Approach:
The strength of drug habits is studied as a function of prior treatment history for alcohol, heroin, cocaine, barbiturates, treatment by a physician, and participation in drug research studies. Of particular interest is the relationship between early reinforcing experiences and later habits. Subjects initially fill out a form detailing drugs used, and days of use for 144 drugs is assessed. Subjects are asked to rate standard drugs plus some drug that they have used, on rating scales that refer to liking the first experience, present habits for a drug, pressure by family or friends to use a drug, strength of their strongest habit, and damage from a drug (addiction). Participants provide written descriptions of first drug experiences, development of a drug habit and/or addiction for a given drug, and treatment history for a variety of drug classes.
Results to Date:
Habits for various drugs vary according to treatment history of users. With respect to first experiences, cigarettes and major tranquilizers are disliked, regardless of treatment group, while cocaine is well liked regardless of treatment group. In drug research subjects, the degree of positiveness or reinforcing value of the first experience is related to ultimate habit strength, while the relationship of liking of the first experience for cigarettes is not related to ultimate habit. Treatment groups also differ on the degree of reinforcement obtained from the first experience of a drug for which treatment was received; alcoholics liked alcohol more on the first trial than addicts liked opiates, and opiate addicts liked heroin more on the first trial than did alcoholics who tried heroin. Use of cigarettes, coffee, and alcohol are related, as are habits of cocaine and heroin use.
Project Dates:
February 1980–June 1986.
Financial Support:
NIDA Addiction Research Center.

0992. FRANCIS SCOTT KEY MEDICAL CENTER, BPRU/Psychiatry D-5-West, 4940 Eastern Avenue, Baltimore, Maryland 21224.

Project Title:
Licit and Illicit Abused Drugs/Behavioral Interaction.

Principal Investigator:
Griffiths, R.R.
Objective:
To study the effects of pharmacological and behavioral manipulations on cigarette smoking in human volunteers.
Methods or Approach:
The two experiments planned will (1) explore drug interactions with cigarette smoking by evaluating the effects on smoking of hydromorphone, naloxone, diazepam, chlorpromazine, caffeine, and carbon monoxide; and (2) extend ongoing research involving a behavioral/pharmacological analysis of the fine grain performance of which smoking is comprised. Studies will characterize within-cigarette changes in puff volume, puff duration, inhalation volume, inhalation duration, and interpuff interval by manipulating length of cigarette, cigarette nicotine delivery, and smoking preloads. Throughout, the self-administration behavior will be monitored by counting the number of cigarettes smoked and by measuring the volume, duration, and distribution of individual cigarette puffs and volume and duration of inhalations with specially constructed devices. Expired air carbon monoxide will be assessed as a physiological measure of smoking. Data will provide an improved understanding of the addictive process by characterizing the interactive relationships between pharmacological and behavioral variables that influence smoking.
Results to Date:
Results are not yet available.
Project Dates:
July 1978–continuing.
Financial Support:
NIDA (DA 03890).

0993. FREDERICK CANCER RESEARCH FACILITY, P.O. Box B, Frederick, Maryland 21701.

Project Title:
Dose–Response Studies With Nitrosomorpholine and Nitrosodiethanolamine, Carcinogenic Constituents of Snuff.

Principal Investigators:
Lijinsky, W.; Kovatch, R.M.
Objective:
To determine carcinogenic effects in rats of very low doses of nitrosamines, at concentrations comparable to those in tobacco.
Methods or Approach:
Nitrosamines were administered to groups of rats in drinking water for 50 or 100 weeks. At the lowest concentrations of nitrosomorpholine (450, 180, and 70 mg/L), groups of 100 rats were used.
Results to Date:
More than 60 percent of animals remain to be examined, but some tumors related to treatment have been seen at all doses.
Project Dates:
November 1982–May 1985.
Financial Support:
NCI (N01CO23909).

0994. JOHNS HOPKINS SCHOOL OF HYGIENE AND PUBLIC HEALTH, 615 North Wolfe Street, Baltimore, Maryland 21205.

Project Title:
Physician-Initiated Smoking Cessation Advice.

Principal Investigators:
Haines, C.S.; Barker, L.R.; Ewart, C.
Objective:
To increase the frequency of physician-initiated smoking cessation advice.
Methods or Approach:
After being trained in a 5-minute smoking cessation advice protocol, internal medicine house officers are provided with patient questionnaires and contract forms in examination rooms while seeing outpatients. Questionnaires have been designed to sequentially prompt the physician to complete the advice quickly and appropriately. Physician behavior is measured by patient report of take-home aids received. Changes in

physician behavior when prompts are withdrawn and then reinstated will be evaluated.

Results to Date:
Project is in a preliminary phase.

Future Plans:
The protocol may be extended to include practicing internists, other physicians who see adult smokers, and nonphysicians.

Project Dates:
July 1984–July 1986.

0995. JOHNS HOPKINS SCHOOL OF HYGIENE AND PUBLIC HEALTH, DEPARTMENT OF HYGIENE, 615 North Wolfe Street, Baltimore, Maryland 21205.

Project Title:
Growing Up: Developmental Epidemiological Studies of Drug and Cigarette Use in Woodlawn.

Principal Investigators:
Kellam, S.G.; Ensminger, M.E.; Brown, C.H.

Objective:
To study how early and evolving family and school structure, social task demands and behavioral responses, and psychological measures work over time to promote, delay, or prevent the use of a variety of substances by adolescents in a particular community.

Methods or Approach:
A prospective longitudinal study of total community populations of Woodlawn children and families was conducted and a followup was done 10 years after the children had been assessed as first graders. The children come from poor, black, urban homes on the south side of Chicago, where the risk of substance abuse is high. The teenagers were given two instruments ("What's Happening?" and "How I Feel"), which measured current social adaptational status and psychological well-being. Comparison populations were first grade children and their mothers who did not participate in the long-term followup (n=302), first graders whose mothers participated in the long-term followup but did not participate themselves (n=325), and a group in which both mothers and children participated (n=704). Social adaptational status and psychological well-being were assessed. Areas of inquiry were drug, cigarette, and alcohol use, evolution of family structure and atmosphere, and delinquency.

Results to Date:
Self-reports indicated a high level of use of all substances except hard drugs (90 percent of subjects had not used hard drugs). Males used all substances except cigarettes more frequently than females. For males, first grade aggressive behavior leads to increased teenage substance use. First grade shyness leads to less substance use later. The combination of aggressiveness and shyness appears to indicate an undersocialized conduct disorder that leads to even higher levels of adolescent substance use among males than aggressiveness without shyness. For females, aggressiveness, shyness, and concentration problems in first grade were not associated with later substance use, except that shyness delays the initiation of use of hard liquor. Underachievement in first grade was related to less substance use in females. Among females, those whose mothers had lower educational expectations for them in first grade used cigarettes more frequently 10 years later. Strong school bonds related to less substance use for both males and females, while strong peer bonds related to more use among males and strong family bonds related to less use among females. Social bonds were clearly related to substance use but not to early adaptation.

Financial Support:
NIDA (1R01DA02591; 5R01DA00787).

References:
(1) Kellam, S.G.; Adams, R.G.; Brown, C.H.; et al. "The Long-Term Evolution of the Family Structure of Teenage and Older Mothers." *Journal of Marriage and Family* 44(3):539-554, 1982. (2) Kellam, S.G.; Brown, C.H.; Rubin, B.R., et al. "Paths Leading to Teenage Psychiatric Symptoms and Substance Use: Developmental Epidemiological Studies in Woodlawn." In: Guze, S.B.; Earls, F.; Barrett, J.E. (Editors). *Childhood Psychopathology and Development.* New York, Raven Press, 1982. (3) Ensiminger, M.E.; Brown, C.H.; Kellam, S.G. "Sex Differences in Antecedents of Substance Use Among Adolescents." *Journal of Social Issues on Women's Use of Drug and Alcohol: New Perspective* 38(2):25-42, 1982. (4) Kellam, S.G.; Brown, C.H.; Fleming, J.P. "Social Adaptation in First Grade and Teenage Drug, Alcohol, and Cigarette Use: Developmental Epidemiological Research in Woodlawn." *Journal of School Health* 52(5):301-306, May 1982.

0996. JOHNS HOPKINS UNIVERSITY, P.O. Box 501, Baltimore, Maryland 21205.

Project Title:
Analysis of Cigarette and Coffee Use Interactions.

Principal Investigators:
Emurian, H.H.; Brady, J.V.; Ray, R.L.

Objective:
To undertake an experimental analysis of the relationships between cigarette-smoking and coffee-drinking habits under laboratory conditions that provide for continuous and comprehensive observations of these habits and other behavioral events.

Methods or Approach:
Observations of instances of cigarette smoking and coffee drinking are undertaken during 10-day residences of three-person groups in a programmed environment that provides for continuous and comprehensive assessment of individual and social behaviors in relationship to a broad range of environmental circumstances (e.g., work, leisure, learning, eating, socializing, etc.) typically involved in everyday life pursuits. Event time-series analyses are employed (1) to assess the dependencies between series of cigarette smoking and coffee drinking under conditions involving abstinence and/or dose manipulations of such commonly used substances, and (2) to assess the dependencies among series of cigarette-smoking, coffee-drinking, and programmed environment activity events under conditions of ad libitum substance use.

Results to Date:
Event time-series analyses have revealed a relationship between cigarette smoking and coffee drinking among habitual users of these substances: coffee-drinking events tended to occur late in the inter-cigarette interval. The substitution of decaffeinated coffee had no effect on the observed relationship, nor did the unavailability of coffee affect the number of cigarettes smoked per day, the mean inter-cigarette interval, and the standard deviation of the inter-cigarette interval. These data suggest that coffee drinking may be one among many stimuli that in combination determine the occurrence in time of cigarette smoking, or that the causal direction in the relationship is from cigarette smoking to coffee drinking, excluding the possible action of other causal agents.

Future Plans:
Multivariate event time-series techniques will be developed for the study of cigarette-smoking and coffee-drinking events in

relationship to concurrent environmental and behavioral events.
Project Dates:
September 1980–1983.
Financial Support:
NIDA (1520595110).

0997. JOHNS HOPKINS UNIVERSITY, SCHOOL OF HYGIENE AND PUBLIC HEALTH, 615 North Wolfe Street, Baltimore, Maryland 21205.

Project Title:
Genetic and Other Factors in Pulmonary Function and Aging.

Principal Investigators:
Cohen, B.H.; Levy, D.A.; Tockman, M.S., et al.
Objective:
To (1) evaluate, summarize, and report pulmonary function characteristics and genetic markers in participants of the Baltimore Longitudinal Study of Human Aging (BLSA); (2) explore relationships among individual and family characteristics (smoking, pulmonary function (PF), α_1-antitrypsin and other genetic markers, familial mortality); (3) develop predictor indices of individual aging, survivorship, and mortality patterns; and (4) relate characteristics to pulmonary function deterioration and to mortality experience of study participants.
Methods or Approach:
The ongoing 24-year BLSA follows a community of adults, free of disease at recruitment, with physiological, psychological, biochemical, clinical, and anthropometric measurements at regular intervals. Demographic and epidemiologic data collected include information on smoking (status, level, and cumulative pack-years), providing a summary of past and current smoking history at the time of each interview. The project involves integration of the various tests, history, and other observations plus data analyses on 945 subjects, some having had as many as 23 followup visits. A multiple regression model, including age, height, and an age–height interaction term, was obtained to predict forced expiratory volume in 1 sec (FEV_1) values over the observed range of ages for 205 never smokers. Using the model, predicted values for the 874 individuals with at least one valid PF test were calculated and the ratio of observed FEV_1 at first spirometry to predicted was used as a measure of PF. Predicted survival functions were obtained by evaluating the proportional hazards model at three arbitrary values of percent FEV (70, 90, and 110 percent of predicted).
Results to Date:
A unique opportunity for longitudinal study of smoking, pulmonary function, and mortality has been provided by this data set; more than 92 percent had one or more valid tests of FEV_1, 80 percent had two or more, and nearly 50 percent have had five or more tests. Among subjects who had two or more tests, almost 50 percent had a time span of more than 8 years between the first and last tests. Almost 90 percent have had more than one smoking history interview; no never smokers reported starting to smoke after entry. Subjects who smoked regularly had poorer FEV values than never smokers; ex-smokers had intermediate values. Smoking also influenced mortality; of the 239 subjects who died during the 24-year followup, there was a significantly higher adjusted mortality among regular smokers than among never smokers. However, while cumulative exposure to cigarette smoke (pack-years) was a significant predictor for mortality, pulmonary function has a definite impact, based on the proportional hazards model.
Project Dates:
1958–continuing.
Financial Support:
NIA.

0998. JOHNS HOPKINS UNIVERSITY, SCHOOL OF HYGIENE AND PUBLIC HEALTH, 615 North Wolfe Street, Baltimore, Maryland 21205.

Project Title:
Genetic-Epidemiologic Characteristics of Smokers and Nonsmokers.

Principal Investigators:
Cohen, B.H.; Menkes, H.A.
Objective:
To (1) explore the basis for observed association between smoking and disease; (2) develop genetic–epidemologic profiles of smokers to examine genetic and environmental (epi-gen) factors responsible for possible indirect associations between smoking and disease; and (3) identify epi-gen factors that may be specific factors (susceptibility or protective) involved in smoking-related pulmonary function/disease interactions.
Methods or Approach:
Participants (adults in a long-term genetic–epidemiologic study of airways obstruction) include a neighborhood population series, an occupational series, and relatives of patients. To explore possible indirect associations, an attempt is being made to determine whether cigarette smokers and nonsmokers differ in epi-gen characteristics that may predispose them to differential morbidity and mortality risks, regardless of smoking habits. To identify possible interactions, examination is being conducted on interrelationships among epi-gen characteristics and smoking with pulmonary function, respiratory symptoms, and disease, to determine if epi-gen characteristics have different effects in individuals with different smoking habits and whether smokers with different epi-gen characteristics show different manifestations. Epi-gen factors under study include genetic marker traits, microenvironmental exposures, and demographic and mixed variables.
Results to Date:
The outcome variable frequency of being a cigarette smoker (>1 pack/day) was examined in relation to 14 epi-gen variables (age, sex, race, socioeconomic status (SES) in terms of median rental, education, Pi (α_1-antitrypsin) type, familial lung disease, ABO type, ABH secretor status, and consumption of coffee, tea, alcohol, diet soda, and milk), each adjusted for all others. Characteristics significantly associated with cigarette smoking appear to be white race, consumption of alcohol and coffee, and a lower educational level. When the interrelationships of each of the epi-gen characteristics and smoking with airways obstruction (AO) as the reference disorder were examined, heavier coffee consumption, being a first-degree relative of a chronic bronchopulmonary disease patient, and surprisingly, being a nondrinker of diet soda appear to be risk factors for AO in smokers but not in never smokers, suggesting an interaction between smoking and each variable. With chronic bronchitis (CB), there was a suggested interaction between milk intake and cigarette smoking; daily milk consumption appears to afford some protective effect against CB in regular daily smokers, although milk intake in never smokers showed no relationship with frequency of CB.
Future Plans:
A longitudinal followup study is planned.
Project Dates:
July 1982–December 1984.
Financial Support:
NHLBI (HL 14153, 1-HR1-2216).

0999. JOHNS HOPKINS UNIVERSITY, DANA CENTER FOR PREVENTIVE OPHTHALMOLOGY, Wilmer Eye Institute, 600 North Wolfe Street, Baltimore, Maryland 21205.

Project Title:
Racial Variations of Chronic Open Angle Glaucoma.

Principal Investigator:
Sommer, A.
Objective:
To (1) determine the source of increased prevalence of glaucomatous blinding in blacks; (2) measure prevalence of glaucomatous visual field loss and ocular hypertension in comparable populations of whites and blacks in East Baltimore; and (3) compare potential risk factors between cases and controls, stratified by race.
Methods or Approach:
Glaucoma is one of the leading causes of blindness in the United States. In whites, it ranks third behind retinal diseases and cataract, with an estimated blindness prevalence of 8.6/100,000. In blacks, it is the leading cause of blindness, with a blindness prevalence of 72.0/100,000, a sevenfold excess over whites. A cluster sample of households in East Baltimore will be selected, and all persons 40 years of age or older residing in those households will be screened for visual field loss and elevated intraocular pressure at neighborhood screening centers. Those who test positively for visual field loss, elevated intraocular pressure, or unexplained reduction of visual acuity will be evaluated at the Wilmer Eye Institute to further define the diagnosis and confirm screening results. Sources of data will include screening and evaluation examinations, anthropometry, blood pressure, and personal interview. Smoking and drinking habits will be examined as risk factors for glaucoma.
Results to Date:
Project is in a preliminary phase.
Financial Support:
NIH (1RO1EY05091-01).
Project Dates:
June 1984–June 1989.

1000. JOHNS HOPKINS UNIVERSITY, SCHOOL OF HYGIENE AND PUBLIC HEALTH, Training Center for Public Health Research, P.O. Box 2067, Hagerstown, Maryland 21740.

Project Title:
Smoking and Mortality in Women.

Principal Investigators:
Bush, T.L.; Comstock, G.
Objective:
To evaluate the effect of cigarette smoking on cardiovascular and cancer mortality in a cohort of women followed prospectively for 12 years.
Methods or Approach:
A cohort of 25,000 white women, residents of Washington County, Maryland, has been followed for 12 years (or until death). Smoking was measured at baseline, as were other possible confounders including educational level and social status. All women ≥ 25 years of age who were residents of the county at baseline were included.
Results to Date:
Cigarette smoking is associated with a significantly increased risk of atherosclerotic heart disease and lung and cervical cancer.
Future Plans:
Results will be published.
Project Dates:
July 1979–June 1985.
Financial Support:
Johns Hopkins University; NHLBI (5T32HL07024; HL 21670); NCI (24758).

1001. JOHNS HOPKINS UNIVERSITY, SCHOOL OF HYGIENE AND PUBLIC HEALTH, Training Center for Public Health Research, P.O. Box 2067, Hagerstown, Maryland 21742-2067.

Project Title:
Serologic Precursors of Cancer.

Principal Investigator:
Comstock, G.W.
Objective:
To investigate the association of serum levels of retinol, beta-carotene, vitamin E, and selenium with respect to demographic and personal characteristics (including smoking history).
Methods or Approach:
Controls for case–control studies of colon and lung cancer were drawn from a population of 26,000 volunteers who donated blood for a serum bank in 1974. Serum has been analyzed for retinol, beta-carotene, vitamin E, and selenium. Substance levels are being analyzed with respect to sex, age, marital status, education, hours after eating, vitamin supplementation, and smoking history.
Results to Date:
Beta-carotene levels showed a downward trend with increasing cigarette consumption. Retinol levels showed a similar trend for males but not for females. There was no association of vitamin E or selenium levels with daily level of cigarette consumption.
Future Plans:
The association between smoking and ulcerative colitis and Crohn's disease will be studied.
Project Dates:
June 1974–continuing.
Financial Support:
NCI (CA 36390).

1002. JOHNS HOPKINS UNIVERSITY, 615 North Wolfe Street, Baltimore, Maryland 21205.

Project Title:
Paths to Adolescent Drug and Mental Health Problems.

Principal Investigator:
Ensminger, M.E.
Objective:
To (1) examine the continuities between early risk factors, evolving family, school, psychological, and individual conditions and teenage outcomes, focusing on predisposing, enhancing, inhibiting, or mediating circumstance; (2) identify antecedents and evolving paths leading to one adolescent outcome with those leading to others (alcohol and drug use, psychiatric symptoms, self-esteem, delinquency); (3) explore how individuals with multiple disorders differ in terms of antecedents and mediating factors from those with a single disorder; and (4) propose intervention strategies, suggested by results, that will identify target subgroups, critical times for interventions, and social fields in which to intervene.
Methods or Approach:
The longitudinal, communitywide project is concerned with examining risk factors early in life that lead to alcohol and drug abuse and mental health (ADM) disorders among adolescents. A population of children and their families were

assessed when the children were in the first grade and again 10 years later. Teacher ratings, clinician's ratings, self-reports, mother's reports, and school records are the sources of data.

Results to Date:

A number of risk factors have been identified, beginning as far back as first grade, for heavy alcohol, drug, and cigarette use, delinquency, and psychological distress during adolescence. The next step is to find factors that mediate between the antecedents and later outcomes and to learn how both factors and the outcomes interact. Knowing how risk factors evolve will be important in identifying targets for prevention and critical points in the child's life for intervention.

Project Dates:

June 1984–June 1986.

1003. JOHNS HOPKINS UNIVERSITY, SCHOOL OF HYGIENE AND PUBLIC HEALTH, Neurotoxibiology Program, 615 North Wolfe Street, Baltimore, Maryland 21205.

Project Title:

Neurotoxicology of Prenatal Carbon Monoxide Exposure.

Principal Investigator:

Fechter, L.D.

Objective:

To determine whether exposure to low levels of carbon monoxide (CO) during gestation disrupts the neurochemical development of the brain; determine threshold dose level at which neurochemical alteration occurs and the time periods during which susceptibility is greatest.

Methods or Approach:

Brain structures to be studied have previously been demonstrated to be highly susceptible to insult produced by severe CO exposure and reductions in oxygen availability in both human autopsy material and animal experiments. Behavioral evidence has been obtained following mild prenatal CO exposure that is consistent with damage to the brain regions. Cell number and cell size in susceptible brain structures will be determined at several time intervals during development to establish whether CO exposure disrupts or delays cell proliferation and growth using protein and nucleic acid assays. Synaptogenesis will be evaluated indirectly by assessing effects of CO exposure on neurotransmitters that innervate these structures and on endogenous neurotransmitters. Direct light microscopic and morphometric analysis will also be conducted.

Results to Date:

It has been determined that perinatal CO exposure in rats produces permanent learning and memory deficits; elevates cerebellar norepinephrine concentration; depresses cerebellar size; and appears to disrupt formation of some GABA-ergic cells. Similarly, CO exposure elevates dopaminergic concentration and content of the neostriatum.

Future Plans:

Studies in progress will determine which cells in the cerebellum are most sensitive to CO exposure and the functional significance of neurochemical changes observed in the cerebellum and neostriatum.

Project Dates:

March 1983–March 1986.

Financial Support:

Health Effects Institute.

1004. JOHNS HOPKINS UNIVERSITY, WILMER OPHTHALMOLOGICAL INSTITUTE, Baltimore, Maryland 21205.

Project Title:

Past and Present Smoking Habits of Patients With Ocular Inflammations.

Principal Investigator:

Knox, D.L.

Objective:

To determine whether patients with different forms of ocular inflammation (iritis, iridocyclitis, pars planitis, optic neuritis) have any distinct and significant smoking habits.

Methods or Approach:

Cross-sectional data on patients and controls are analyzed for age and gender distribution of former and current cigarette, cigar, and pipe smoking habits.

Results to Date:

Among patients with pars planitis, 68 percent of males and 61 percent of females were current smokers compared with 37 percent of males and 40 percent of females among controls; odds ratios and p values were 2.92 and 0.01 for males and 2.61 and 0.015 for females. Among patients who smoked, 57 percent of males and 36 percent of females smoked >20 cigarettes/day; among controls, 25 percent of males and 24 percent of females smoked >20 cigarettes/day. Odds ratios and p values were 3.49 and 0.001 for men and 2.39 and 0.045 for women.

Project Dates:

November 1971–continuing.

Financial Support:

Johns Hopkins University, Wilmer Ophthalmological Institute.

1005. JOHNS HOPKINS UNIVERSITY, SCHOOL OF HYGIENE AND PUBLIC HEALTH, COEH, 3100 Wyman Park Drive, Building 6, Baltimore, Maryland 21211.

Project Title:

Different Risk Factor Distributions for Airways Obstruction and Chronic Bronchitis.

Principal Investigators:

Tockman, M.S.; Khoury, M.J.; Cohen, B.H.

Objective:

To determine whether risk factor distributions differ for airways obstruction and chronic bronchitis.

Methods or Approach:

Cross-sectional data of 2,539 adult nonpatient participants in a genetic-epidemiologic study of pulmonary function were analyzed. Airways obstruction (AO) was defined as forced expiratory volume in 1 sec of <68 percent of forced vital capacity. Chronic bronchitis (CB) was identified by questionnaire report of cough and sputum production for 3 or more months/year for 2 consecutive years.

Results to Date:

AO was present in 13.4 percent of subjects, CB in 11.9 percent. AO and CB were present in 3.5 percent. Observed frequencies of AO and CB were simultaneously adjusted for 16 variables by multiple linear regression. AO was significantly associated with advanced age, male sex, PiZ allele, blood group A antigen, heavy coffee intake (>3 cups/day), and first degree relationship to a patient with chronic obstructive pulmonary disease. Neither age, sex, Pi type, nor other AO risk factors contributed to (adjusted) frequency of CB. Both AO and CB were associated with cigarette smoking and low socioeconomic status. Data indicate that although cigarette smoking and low socioeconomic status are common to AO and CB, other host and environmental characteristics distribute differently between those at risk of obstruction and those at risk of bronchitis. Distinctions may be useful in understanding the separate pathogenetic processes and subsequent natural histories of AO and CB.

Financial Support:
NHLBI (HL14153); CTR (1476).

1006. JOHNS HOPKINS UNIVERSITY, SCHOOL OF HYGIENE AND PUBLIC HEALTH, COEH, 3100 Wyman Park Drive, Building 6, Baltimore, Maryland 21211.

Project Title:
Airways Obstruction and the Risk of Lung Cancer.

Principal Investigators:
Tockman, M.S.; Anthoisen, N.R.; Wright, E.C.

Objective:
To determine whether airways obstruction increases the risk of lung cancer.

Methods or Approach:
Data from the Intermittent Positive Pressure Breathing (IPPB) study and from the Johns Hopkins Lung Project (JHLP) were analyzed to determine degree of airways obstruction and magnitude of lung cancer risk. Age, smoking, and ventilatory status were determined at study entry.

Results to Date:
Data show that airways obstruction increases the risk of lung cancer. The association was seen in the JHLP group alone and in the combined JHLP-IPPB populations. The magnitude of the airflow obstruction/lung cancer risk (odds ratio = 5.31), absence of other factors with an odds ratio of similar magnitude, and variety of analyses demonstrating the association support the validity of obstruction as a major lung cancer risk factor. Significant cross-sectional association of age and pack-years of smoking were found with airflow obstruction. After log-linear adjustment for cross-sectional associations, development of lung cancer no longer depended on age. Prospective contribution of pack-years to development of lung cancer was reduced by cross-sectional adjustment, but remained significant. Importantly, the prospective risk of airflow obstruction for subsequent development of lung cancer had an odds ratio two to three times the odds ratio for pack-years. Among obstructed male smokers, lung cancer risk is significantly in excess of that observed among nonobstructed, and increasing the degree of airflow obstruction increases the risk of lung cancer. Data suggest that smokers who will develop lung cancer may be recognized by prior development of ventilatory obstruction.

Project Dates:
March 1984–September 1984.

Financial Support:
NHLBI (N01HR72901; N01HR72902; N01HR72903; N01-HR72904; N01HR72905; N01HR72906); NCI (N01CN45037; M01RR0035021; M01RR0072).

1007. JOHNS HOPKINS UNIVERSITY, SCHOOL OF HYGIENE AND PUBLIC HEALTH, COEH, 3100 Wyman Park Drive, Building 6, Baltimore, Maryland 21211.

Project Title:
Milk Drinking and Possible Protection of the Respiratory Epithelium.

Principal Investigators:
Tockman, M.S.; Khoury, M.J.; Cohen, B.H.

Objective:
To determine whether the presence of an airways insult (cigarette smoking) might affect prevalence of chronic bronchitis (CB) in individuals with low intake of Vitamin A.

Methods or Approach:
The association between milk ingestion and prevalence of CB was investigated in 2,539 nonpatient adult participants in a genetic-epidemiologic study of pulmonary function, via detailed interviews and spirometry. CB was identified by report of cough and phlegm production for ≥ 3 months/year for 2 consecutive years.

Results to Date:
A significantly higher prevalence of CB was found among subjects who did not drink milk: 17.7 percent of nondrinkers compared with 11.7 percent of milk drinkers. The difference persisted after binary multiple regression adjustment for cigarette smoking, forced expiratory volume in 1 sec, and other potentially confounding variables including age, sex, race, socioeconomic status, education, and alcohol and coffee intake. No reduction in CB prevalence was seen in the absence of airways insult. Among nonsmoking adults, nondrinkers had adjusted CB prevalence of 6.0 percent, not significantly different from adjusted CB prevalence of daily milk drinkers (6.7 percent). In contrast, regular cigarette smokers ($\geq$ 1 pack/day) who did not drink milk had a significantly higher adjusted rate of CB (31.7 percent) than regular smokers who were also daily milk drinkers (20.2 percent). Difference was not due to difference in smoking history; mean pack-years for milk drinkers was 31.1 compared with 29.9 for nondrinkers who smoked. However, further confirmation is required that Vitamin A in milk is responsible for the inverse relationship between CB and milk ingestion, and that Vitamin A ingestion is protective against subsequent bronchitis.

Financial Support:
NHLBI (HL 14153); CTR (1476).

Reference:
Cohen, B.H. "Chronic Obstructive Pulmonary Disease: A Challenge in Genetic Epidemiology." *American Journal of Epidemiology* 112:274-288, 1980.

1008. JOHNS HOPKINS UNIVERSITY, FRANCIS SCOTT KEY MEDICAL CENTER, 4940 Eastern Avenue, Baltimore, Maryland 21224.

Project Title:
Behavioral Methods for Cigarette Smoking Reduction.

Principal Investigator:
Stitzer, M.L.

Objective:
To develop and test an objectively verified, quantifiable clinical method for reducing cigarette smoking by chronic smokers.

Methods or Approach:
Expired carbon monoxide (CO) was evaluated as a target for reinforcement intervention in 11 volunteer smokers in a 3-week study which utilized an A-B-A design. CO levels were measured on weekday afternoons and detailed self-report records of smoking were kept by subjects throughout the study. A monetary payment of 5 dollars was available during study week 2 for CO readings which were 50 percent or less of the average reading obtained for that subject during study week 1. Contingent payment was withdrawn during study week 3.

Results to Date:
Three measures of smoking changed in an orderly manner during the study. CO readings were reduced from initial

baseline levels during study week 2, but generally did not return to original baseline levels when the contingency was withdrawn. Number of daytime cigarettes recorded decreased and minutes of cigarette abstinence prior to the afternoon study contact increased during the contingent intervention period compared with baseline study phases. The average within-subject correlation between expired air CO level and number of daytime cigarettes was 0.67 ($p<0.01$), that between CO and time since last cigarette was -0.59 ($p<0.05$).

Project Dates:
April 1980–November 1986.

Financial Support:
NIDA (5R0103893-02XO).

Reference:
Stitzer, M.L.; Bigelow, G.E. "Contingent Reinforcement for Reduced Carbon Monoxide Levels in Cigarette Smokers." *Addictive Behaviors* 7(4):403-412, 1982.

1009. NATIONAL CANCER INSTITUTE, Landow Building 3C09, Bethesda, Maryland 20205.

Project Title:
Pipes, Cigars, and Smokeless Tobacco in Relation to Bladder Cancer.

Principal Investigators:
Hartge, P.; Hoover, R.; Kantor, A.

Objective:
To assess the role of noncigarette tobacco in bladder cancer etiology.

Methods or Approach:
A case–control interview study was conducted with 2,982 cases and 5,782 controls from the total population of 10 geographic areas of the United States in 1978. Interview data were used to estimate bladder cancer incidence ratios according to exposure to noncigarette tobacco.

Results to Date:
Compared with men who had never smoked, men who smoked pipes (but not cigars) had an incidence ratio estimated as 1.23 (95 percent confidence interval, CI, 0.75-2.00); those who smoked cigars (but not pipes) were estimated to have an incidence ratio of 1.33 (95 percent CI, 0.92-1.94). Little evidence of dose response was seen. The excess risk in pipe smokers was limited to those who inhaled deeply.

Project Dates:
September 1977–1987.

Financial Support:
NCI; FDA.

1010. NATIONAL CANCER INSTITUTE, Landow Building 3C09, Bethesda, Maryland 20205.

Project Title:
Role of Cigarette Smoking in Bladder Cancer.

Principal Investigators:
Hartge, P.; Hoover, R.; Silverman, D., et al.

Objective:
To assess the specific relationships between bladder cancer risk and timing, intensity, and type of cigarette exposure.

Methods or Approach:
Interview data from a population-based case–control study of bladder cancer were used to estimate the relative risk of bladder cancer according to various measures of cigarette smoking.

Results to Date:
The risk of bladder cancer was more than twice as high in smokers compared with nonsmokers. Detailed analyses of type of cigarette exposure are being conducted.

Project Dates:
September 1977–1987.

Financial Support:
NCI; FDA.

1011. NATIONAL CANCER INSTITUTE, Environmental Epidemiology Branch, Occupational Studies Section, Landow Building, Room 4C18, Bethesda, Maryland 20205.

Project Title:
Study of Smoking Among World War I Veterans.

Principal Investigators:
Hrubec, Z.; Blair, A.; Rogot, E., et al.

Objective:
To assess long-term mortality in relation to various forms of tobacco use in veterans of World War I.

Methods or Approach:
In 1954, a roster of World War I veterans was assembled to be followed for mortality through Government life insurance policies. Information on smoking, occupation, industry, and place of residence was obtained through a mailed questionnaire and has been analyzed periodically with accumulated mortality data. A group of 293,958 owners of Government life insurance policies that were active in 1953 have been followed through the Veterans Administration, which handled this insurance. Addresses obtained through the insurance program were used to mail questionnaires in 1954 and again in 1957 to nonrespondents. A total of 84 percent of the roster provided some information on the questionnaire. Periodic evaluation has been by standard epidemiologic methods.

Results to Date:
Findings, first reported in 1959, gave one of the earliest indications of the association between lung cancer and smoking (obtained in a cohort study). Various other cancers and cardiovascular diseases were found to be related to smoking in that analysis and in a subsequent study at 8.5-year followup that focused on the effects of smoking cessation. A more recent evaluation at 16-year followup confirmed earlier findings, with the following mortality ratios for current cigarette smokers compared with nonsmokers: all causes, 1.73; cancer, all sites, 2.12; lung cancer, 11.28; coronary heart disease, 1.58; and bronchitis and emphysema, 12.07.

Future Plans:
Cause-specific mortality of various occupational groups is being evaluated with control of smoking as a covariable. Geographic variation in cause-specific mortality will be examined while controlling for occupational and industrial exposures and smoking.

Project Dates:
1953–continuing.

Financial Support:
NCI.

Reference:
Rogot, E.; Murray, J.L. "Smoking and Causes of Death Among U.S. Veterans: 16 Years of Observation." *Public Health Reports* 95:213-222, 1980.

1012. NATIONAL INSTITUTE ON DRUG ABUSE, ADDICTION RESEARCH CENTER, P. O. Box 5180, Baltimore, Maryland 21224.

Project Title:
Behavioral Pharmacology of Nicotine.

Principal Investigators:
Henningfield, J.E.; Jasinski, D.R.
Objective:
To (1) determine the pharmacologic profile of nicotine as a drug with suspected dependence-producing activity; (2) investigate the role of nicotine in the behavior and effects of cigarette smoking; and (3) examine the utility of pharmacologic approaches for the treatment of tobacco dependence.
Methods or Approach:
Human volunteers are studied on a residential research ward during 3- to 12-week studies of three general types: (1) behavioral, subjective, and physiologic effects of nicotine are assessed following administration via i.v., s.c., and s.l. routes, smoke inhalation, and nicotine gum chewing; (2) an i.v. nicotine self-administration paradigm is used to assess the positive and negative reinforcing properties of nicotine and the development of tolerance to such activity; and (3) cigarette smoking behavior is measured following administration of various drugs.
Results to Date:
Intravenous nicotine produces many of the effects of nicotine delivered by tobacco smoke inhalation and other routes of nicotine administration. Many effects of nicotine are biphasic, onsetting within seconds of administration (e.g., bradycardia, pupil dilation, euphoria) and reverse within a few minutes. Nicotine serves as either a positive or a negative reinforcer as a function of dose and other parameters. At physiologically inactive doses, mecamylamine attenuates subjective effects of nicotine. Cigarette smoking rates vary as a function of drug administration, e.g., morphine enhances and nicotine inhibits cigarette smoking. The behavioral pharmacologic profile of nicotine is that of a prototypic dependence-producing drug, similar in key respects to cocaine and morphine.
Future Plans:
Objectives of future studies will be to (1)investigate two specific pharmacologic treatments for tobacco dependence–nicotine preloading using nicotine chewing gum ("methadone" strategy), and nicotine antagonism using selective ganglionic blockers ("naltrexone" strategy); (2) quantify the suspected tobacco withdrawal syndrome using approaches previously validated for assessing withdrawal from other drugs; (3) continue behavioral pharmacologic studies of nicotine dependence; and (4) study effects of nicotine on electrophysiologic responses, and performance on behavioral and cognitive functioning.
Project Dates:
1980–continuing.
Financial Support:
NIDA.

1013. NATIONAL INSTITUTE ON DRUG ABUSE, ADDICTION RESEARCH CENTER, P.O. Box 5180, Baltimore, Maryland 21224.

Project Title:
A Comparison of Nicotine and Cocaine Self-Administration in the Dog: Fixed-Ratio and Progressive-Ratio Schedules of Intravenous Drug Infusion.

Principal Investigators:
Risner, M.E.; Goldberg, S.R.
Objective:
To (1) compare behavior maintained by nicotine or cocaine infusions delivered under a fixed-ratio schedule of reinforcement; (2) assess relative reinforcing properties of nicotine and cocaine in a progressive-ratio procedure; (3) assess effects of presession treatment with mecamylamine on nicotine and cocaine self-administration; and (4) quantify direct physiological effects of nicotine in conscious dogs.
Methods or Approach:
Beagle dogs were surgically fitted with chronic venous catheters and given access to response-contingent drug infusions under a fixed-ratio 15, timeout 4-min schedule of reinforcement. In another study, catheterized beagle dogs pressed a lever under a progressive-ratio schedule of drug infusions. Under this schedule, the response requirement was increased daily until the dog failed to complete the necessary fixed-ratio. Catheterized beagle dogs that had stable rates of responding for nicotine or cocaine were treated with the nicotine antagonist mecamylamine for several consecutive sessions. Effects of i.v. nicotine on heart rate, rectal temperature, and pupil diameter were measured in loosely restrained, conscious dogs at timed intervals following drug administration.
Results to Date:
Both nicotine and cocaine were self-administered above saline levels, with the maximum number of infusions occurring at a dose of 30 μg/kg nicotine and 100 μg/kg cocaine. Rates of responding first increased, reaching a maximum at 10 to 30 μg/kg/infusion, and then decreased as the dose of nicotine or cocaine was varied between 3 and 300 μg/kg/infusion. Rate of responding and number of infusions obtained per session were higher under the schedule of cocaine self-administration than under the schedule of nicotine self-administration. Presession treatment with mecamylamine decreased nicotine-maintained responding to levels not unlike those seen when saline was substututed for the drug. Neither cocaine- or water-maintained responding was affected by presession treatment with mecamylamine. Under the progressive-ratio schedule, the maximum fixed-ratio value at which responding was maintained first increased as the dose per infusion increased and then, at the highest dose, either remained the same or decreased. Cocaine maintained considerably higher fixed-ratio values than nicotine, but maximum fixed-ratio values were well above those seen with saline. Nicotine produced dose- and time-related changes in heart rate, rectal temperature, and pupil diameter. Effects of mecamylamine were considerably greater than effects of nicotine.
Project Dates:
July 1979–June 1983.
Financial Support:
NIDA.

1014. NATIONAL INSTITUTE ON DRUG ABUSE, ADDICTION RESEARCH CENTER, P.O. Box 5180, Baltimore, Maryland 21224.

Project Title:
Effects of Nicotine, Cocaine, and Their Metabolites on Schedule-Controlled Responding by Beagle Dogs and Squirrel Monkeys.

Principal Investigators:
Risner, M.E.; Goldberg, S.R.; Prada, J.A., et al.
Objective:
To characterize effects of cocaine and its N-demethylated metabolite norcocaine on schedule-controlled responding maintained by food presentation in beagle dogs; determine effects of nicotine and two of its metabolites, nornicotine and cotinine, on schedule-controlled responding in dogs and squirrel monkeys.
Methods or Approach:
Using operant conditioning procedures, beagle dogs and squirrel monkeys responded under a multiple fixed-interval (FI) 300-second, fixed-ratio (FR) 30 response schedule of food

presentation. Sessions were conducted daily, Monday through Friday. Drug experiments began when rates and temporal patterns of responding were stable. Graded doses of cocaine and norcocaine in beagle dogs and nicotine, nornicotine, and cotinine in beagle dogs and squirrel monkeys were administered intramuscularly no more than twice/week. Control injections were administered once/week.

Results to Date:
Nicotine (0.01 to 1.0 mg/kg) and nornicotine (0.03 to 3.0 mg/kg) produced qualitatively similar effects in dogs and monkeys. Nicotine produced dose-related increases and then decreases in rates of responding during FI components; rates of responding during FR components were only decreased. Nornicotine produced only dose-dependent decreases in responding during both FI and FR components. In dogs, cotinine (0.01 to 10.0 mg/kg) produced only dose-dependent decreases during FI and FR components; however, in squirrel monkeys, cotinine (0.1 to 3.0 mg/kg) increased responding during FI components, and high doses of 30.0 mg/kg decreased responding during FI and FR components. Behavioral effects of cocaine (0.03 to 3.0 mg/kg) and norcocaine (0.01 to 1.0 mg/kg) were compared. FI rates of responding first increased and then decreased with increasing doses of each drug. Norcocaine was slightly more potent than cocaine in producing effects on schedule-controlled responding in dogs.

Future Plans:
Studies will assess effects of stereoisomers of nicotine and nornicotine on schedule-controlled behavior. Physiologic and pharmacokinetic profiles of the compounds are also being assessed. Results will help elucidate the mechanism of action, especially with regard to stereoselectivity.

Project Dates:
January 1983–June 1985.

Financial Support:
NIDA.

1015. PRINCE GEORGES COUNTY PUBIC SCHOOLS, 7711 Livingston Road, Oxon Hill, Maryland 20904.

Project Title:
Smoking Deserves a SMART Answer.

Principal Investigator:
Largay, B.P.

Objective:
To evaluate a new intervention program designed for grades 4, 5, and 6.

Methods or Approach:
Field testing had determined that the program had a positive impact. Pretests and posttests were used and an attitudinal survey was conducted.

Results to Date:
The project appears to make a positive and significant difference in how students respond to students and how they handle smoking vs. nonsmoking.

Project Dates:
February 1983–February 1985.

Financial Support:
Prince Georges County Public Schools; ALA of Maryland.

1016. THE FRANKLIN INSTITUTE, 4701 Willard Avenue, Suite 310, Chevy Chase, Maryland 20815.

Project Title:
Cigarette Switch Follow-Up Study.

Principal Investigators:
Lynch, C.J.; Gori, G.B.

Objective:
To measure the extent to which smoking patterns changed for smokers who had voluntarily switched brands over a long period of time, unencumbered by experimental protocol.

Methods or Approach:
Plasma cotinine, expired air carbon monoxide, blood carboxyhemoglobin, daily cigarette consumption, and other parameters are available for over 2,000 smokers who participated in previous smoking-related studies. All smokers will be contacted and approximately 200 of those who have switched brands in the interim will be retested; 100 previous participants who have not switched brands will serve as controls. Data should provide a basis for estimating changes in smoking patterns for those who voluntarily switched brands over a long period of time (at least 2 years) as part of adopted smoking history. Particular emphasis will be placed on smokers who have switched to FTC lower yield brands.

Results to Date:
Results are not yet available.

Future Plans:
Additional followup of smokers is anticipated in 2 to 3 years.

Project Dates:
December 1984–June 1985.

Financial Support:
NCI (1R01CA38640-01).

1017. THE FRANKLIN INSTITUTE, 4701 Willard Avenue, Suite 310, Chevy Chase, Maryland 20815.

Project Title:
Smoker Compensation and Cigarette Smoke Yield.

Principal Investigators:
Lynch, C.J.; Gori, G.B.; Benowitz, N.L.

Objective:
To determine the extent to which smokers alter smoking patterns after switching from customary brands to cigarettes of different FTC yields of tar, nicotine, and carbon monoxide (CO).

Methods or Approach:
Seventy-two volunteers who currently smoke cigarettes yielding 14 to 16 mg tar will participate over a 12-week period. Baseline data will be obtained during the first 2 weeks. Volunteers will then switch sequentially to five other brands, each having FTC lower tar, nicotine, and CO yields. Alternative brands will be smoked for a 2-week period. Weekly measurements will be taken of cigarette consumption, plasma nicotine and cotinine, blood carboxyhemoglobin, expired air CO, and plethysmographic puff profile parameters.

Results to Date:
Results are not yet available.

Project Dates:
October 1984–December 1985.

Financial Support:
NCI (5N01CP31047-01).

1018. UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES, 4301 Jones Bridge Road, Bethesda, Maryland 20814.

Project Title:
Metabolic Activations of Monomethylbenz(*a*)anthracenes.

Principal Investigator:
Yang, S.K.

Objective:
To study the possible differences in metabolic pathways which

can account for the relative carcinogenic potencies of the 12 monomethylbenz(*a*)anthracenes (MBAs).

Methods or Approach:
The proposed research will be carried out in six stages: (1) synthesis of unlabeled and tritium-labeled MBAs by established and newly developed methods; (2) detailed metabolism studies of each MBA in liver, lung, and skin microsomes and homogenates from untreated, phenobarbital- and 3-methylcholanthrene-treated rats and mice; (3) identification of metabolites derived enzymatically from each MBA and purified by high performance liquid chromatography and by physicochemical methods such as ultraviolet and fluorescence spectrophotometry, mass spectrometry, nuclear magnetic resonance spectrometry, and spectropolarimetry; (4) large-scale preparations of MBA metabolites by enzymatic and/or ascorbic acid-ferrous sulfate-EDTA methods; (5) mutagenicity tests of MBA and metabolites with *Salmonella typhimurium* strain TA100 and with Chinese hamster V79 cells; and (6) tumor-initiating activities of the MBAs and their metabolites on mouse skin.

Results to Date:
Many metabolites of MBAs have been identified including several dihydrodiols formed at the methyl-substituted aromatic double bond.

Future Plans:
Studies of mutagenicity and tumor-initiating activities of the MBAs and their metabolites are planned.

Project Dates:
August 1981–July 1985.

Financial Support:
NCI (CA29133).

1019. UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES, SCHOOL OF MEDICINE, Department of Preventive Medicine and Biometrics, 4301 Jones Bridge Road, Bethesda, Maryland 20814.

Project Title:
Cancer in Mormons by Church Activity Measures.

Principal Investigators:
Gardner, J.W.; Lyon, J.L.

Objective:
To determine cancer rates by site for Latter Day Saints (LDS) church members (Mormons) in Utah according to level of participation in church activities and adherence to church health codes which include abstinence from use of alcohol, tobacco, coffee, and tea.

Methods or Approach:
Level of church participation is determined for Mormon cancer patients in Utah who have died, from existing records, including obituaries, and is used to compare cancer rates by level of church participation. Cancer patients are identified from the Utah Cancer Registry. Populations are determined from Utah and LDS church census reports.

Results to Date:
Smoking-associated cancers have much lower rates in Mormons who are active in church affairs. These include cancers of the lung, oral cavity, larynx, pharynx, and bladder. In addition, stomach cancer and several female cancers have low rates in active Mormons.

Future Plans:
Further analysis of data and expansion of study size are being conducted. Better measures of church participation are also being explored.

Project Dates:
June 1978–1984.

1020. UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES, 4301 Jones Bridge Road, Bethesda, Maryland 20814-4799.

Project Title:
Nicotine, Body Weight, and Food Consumption.

Principal Investigator:
Grunberg, N.E.

Objective:
To determine behavioral factors that contribute to the inverse relationship between cigarette smoking (and nicotine administration) and body weight; determine biological mechanisms involved in behavioral factors.

Methods or Approach:
Human and animal (rat) studies include behavioral measures (e.g., food consumption and physical activity) and biological measures (e.g., body weight and endocrine changes). Human studies include smokers and nonsmokers. Rat studies use miniosmotic pumps to administer nicotine.

Results to Date:
Cigarette smoking and nicotine administration are accompanied by decreased consumption of sweet foods with no changes in consumption of nonsweet foods. After cessation of smoking or nicotine administration, there are marked increases in consumption of sweet foods. These changes in specific food consumption appear to contribute to the changes in body weight following cessation of smoking or nicotine administration.

Future Plans:
Specific nutrients, sex differences, and biological mechanisms involved in the effects of nicotine on body weight will be examined.

Project Dates:
October 1981–September 1987.

Financial Support:
USUHS; DOD.

1021. UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES, Department of Medical Psychology, 4301 Jones Bridge Road, Bethesda, Maryland 20814.

Project Title:
Endocrinological Responses to the Administration of Nicotine: Interactions With Drug Initiation, Conditioned Effects, and Conditions of Stress.

Principal Investigator:
Morse, D.E.

Objective:
To investigate effects of chronic intermittent intravenous administration of nicotine on several endocrinological and biochemical parameters that may contribute to the physiological determinants and health consequences of cigarette smoking.

Methods or Approach:
Measurements were made of plasma concentrations of catecholamines (norepinephrine, epinephrine, and dopamine), corticosterone, glucose, and insulin, which have been shown to contribute to (1) reinforcement of drug-taking behaviors during development and maintenance of cigarette smoking; (2) decreased body weight among smokers; (3) increased incidence of cardiovascular disorders among smokers; and (4) responses induced by noxious environmental stimuli (stress response). Three aspects of the role of nicotine in tobacco use were examined: effects during drug initiation (phase I); conditioned drug responses (phase II); and reduction of stress-induced

responses (phase III). Using a repeated measures design, test animals (New Zealand white rabbits *Oryctolagus cuniculus*) were surgically prepared with chronic indwelling intravascular cannulae that were used for drug administration and plasma acquisition. Each animal received one dose of nicotine (0.025 mg, 0.05 mg, or 0.10 mg nicotine base/kg body weight) or physiological saline solution throughout the experiment. Drug infusions were made at 2-hour intervals 4 times/day for 13 days.

Results to Date:

In phase I, nicotine administration resulted in increases in plasma concentrations of catecholamines, corticosterone, and glucose and in decreased concentrations of insulin. The magnitude of the norepinephrine and epinephrine responses decreased during the first week, while all other responses were relatively similar in "naive" and nicotine "experienced" (tolerant and/or habituated) animals. These nicotine-induced responses may reinforce development and maintenance of cigarette smoking behavior (and may mediate lower body weight apparent in smokers) by altering level of physiological and/or endocrinological activity (level of arousal) or state of hunger/satiety experienced by the smoker. Increasing doses of nicotine resulted in increasing plasma concentrations of catecholamines and corticosterone, which have been implicated as potential mediators of several cardiovascular disorders. Preliminary evidence suggests a positive relationship between nicotine and histological indications of myocardial degeneration and failure. Phase II data demonstrated that repetitive administration of nicotine in conjunction with simultaneous presentation of a nondrug stimulus (flashing lights) results in development of both conditioned opponent and primary process responses, which may contribute to the tobacco abstinence and withdrawal syndromes. Appropriate presentation of conditioned stimuli (and subsequent elicitation of conditioned response) may be of benefit in reducing discomfort associated with abstinence and withdrawal by substituting for drug administration. Phase III results indicate that presentation of noxious stimulation increases plasma concentrations of norepinephrine, epinephrine, and corticosterone. Nicotine administration to nicotine-experienced animals did not reduce intensity of physiological responses to noxious stimulation; concurrent administration resulted in a somewhat greater intensity of responding than was induced by application of the stressor alone, suggesting that the reported stress-ameliorating effects of smoking are probably not based on reduction of stress-related peripheral physiological processes.

Project Dates:

January 1983–April 1984.

Financial Support:

USUHS.

1022. UNIVERSITY OF MARYLAND, SCHOOL OF MEDICINE, Department of Epidemiology and Preventive Medicine, 655 West Baltimore Street, Baltimore, Maryland 21201.

Project Title:

Followup of the Growth and Development of Children.

Principal Investigators:

Sexton, M.; Hebel, J.R.

Objective:

To determine whether provision of help with smoking cessation and a decrease in smoking during pregnancy results in long-term benefits to growth and development of the child.

Methods or Approach:

The cohort includes approximately 775 3-year-old children whose mothers smoked ≥ 10 cigarettes/day at the beginning of pregnancy and who participated in a randomized clinical trial that included antismoking advice. Data on maternal smoking were validated with a biochemical marker of smoking obtained early and late in pregnancy. Information on physical growth, morbidity, and cognitive and behavioral development of each child is being determined with tests and questionnaires, including the Minnesota Child Development Inventory, the McCarthy Scales of Children's Abilities, measures of physical growth, and history of morbidity. Information regarding current maternal smoking habits is also being obtained. Followup of children at age 3 years and analysis of data will be completed this year.

Results to Date:

Results are not yet available.

Project Dates:

August 1982–July 1985.

Financial Support:

NICHHD (HD 15861-03).

1023. UNIVERSITY OF MARYLAND, SCHOOL OF MEDICINE, Department of Epidemiology and Preventive Medicine, 655 West Baltimore Street, Baltimore, Maryland 21201.

Project Title:

Consequences of Alcohol Consumption During Pregnancy.

Principal Investigator:

Fox, N.L.

Objective:

To assess consequences of low to moderate levels of maternal alcohol consumption prior to and during pregnancy on pregnancy outcome and progress of early childhood development; study interactions between maternal alcohol consumption and smoking.

Methods or Approach:

The prospective epidemiologic study is based on maternal alcohol comsumption and smoking habit data obtained during pregnancy and 3 years postpartum. Approximately 775 children whose mothers smoked ≥ 10 cigarettes/day at the beginning of pregnancy and participated in a randomized clinical trial of antismoking advice constitute the study cohort. Followup data on mental and physical development at 3 years of age are being analyzed to assess consequences of maternal alcohol consumption, patterns and changes in alcohol intake during pregnancy, and relationship between alcohol use and smoking during pregnancy.

Results to Date:

Preliminary analyses confirm that (1) most women reduce alcohol consumption during pregnancy; (2) smoking and alcohol habits during pregnancy are associated; and (3) women who drink beer, wine, or liquor differ in ways important to the risk of low birth weight and other outcomes of pregnancy. Final analyses will be completed in 1986.

Project Dates:

November 1983–August 1986.

Financial Support:

NIAAA (1R23AA06105-01).

1024. UNIVERSITY OF MARYLAND, SCHOOL OF MEDICINE, 29 South Greene Street, Baltimore, Maryland 21201.

Project Title:

Pulmonary Function Adaptation to Ozone in Subjects With Chronic Bronchitis.

Principal Investigators:
Kulle, T.J.; Kerr, H.D.
Objective:
To determine if smokers with chronic bronchitis are sensitive to ozone, if they adapt, and if the adaptation lasts longer than 4 days.
Methods or Approach:
The study was conducted over a 3-week period with each subject (n=20) acting as his or her own control. The subjects breathed filtered air for 3 hrs/day on Thursday and Friday of Week 1 (Control Week), were exposed to 0.41 ppm O_3 for 3 hrs/day on Monday through Friday of Week 2 (Exposure Week), and on Week 3 (Post-exposure/Re-exposure Week), breathed filtered air on Monday, then were re-exposed to 0.41 ppm O_3 on Tuesday. The subjects were studied in groups of 2 to 4. All subjects were asked to abstain from smoking 2 hours prior to entering the chamber and were confined to the Class 100 clean room 1/2 hour prior to each control and exposure period. Every day, 1 hour prior to conclusion of each exposure and control period, bicycle ergometer exercise was performed at a workload of 100 W (612 kg-m/min) at 60 RPM for 15 minutes. Spirometric measurements (FVC, FEV_1, FEV_3) were performed daily at the conclusion of each control and exposure period.
Results to Date:
There were significant decrements in FVC and FEV_1 on the first day of the 5-day repeated exposures, with no significant differences from control during the second through fifth exposure days. When the subjects were re-exposed to ozone 4 days after the sequential exposures, significant decreases in FVC and FEV_1 were again seen. Symptoms were mild with throat irritation and increased coughing predominating. These results suggest that individuals with chronic bronchitis adapt rapidly to ozone and lose this adaptive phenomenon within 4 days. The small decreases seen in FVC and FEV_1 ($\leq$ 3 percent) appear to impose no more than minimal limitations on their daily activities.
Project Dates:
November 1981–1982.
Financial Support:
EPA (R 807 262 02).

1025. UNIVERSITY OF MARYLAND, SCHOOL OF MEDICINE, 655 West Baltimore Street, Baltimore, Maryland 21201.

Project Title:
Environmental Risk Factors in Congenital Heart Disease (Human).

Principal Investigator:
Ferencz, C.
Objective:
To identify new risk factors for cardiac abnormalities which may result from interactions of multiple teratogenic agents or enhancements of fetal damage by nonteratogenic substances.
Methods or Approach:
Index cases will be 2,000 infants with severe congenital heart disease identified over a 6-year period through the Regional Pediatric Cardiology Services in Baltimore and Washington, D.C. Control infants will be chosen at random from the births occurring in area hospitals served by the cardiology centers. Information is obtained by home interviews. A precoded questionnaire administered to the mother records details of pre- and post-conception exposures to drugs, smoking, alcohol, and caffeine. Home environmental exposures caused by heating and cooking fuels, maintenance activities (paints, insecticides), and crafts and hobbies (solvents, lacquer) are noted. Occupational histories of mother and father are examined. Analyses by multiple logistic regression will seek to elucidate additive and interactive effects of the various exposures, after adjustment for confounding variables. Because the multifactorial origin of congenital malformations is widely accepted, a summation or enhancement of environmental insults in the pathogenesis of congenital heart disease is a reasonable possibility.
Results to Date:
Project is on-going and analyses are being made on the first half of the data set.
Project Dates:
December 1980–1988.

1026. UNIVERSITY OF MARYLAND, SCHOOL OF MEDICINE, 655 West Baltimore Street, Baltimore, Maryland 21201.

Project Title:
Pilot Study on the Natural History of Bladder Papilloma.

Principal Investigators:
Kessler, I.I.; Mabuchi, K.; Eggleston, J.C.
Objective:
To investigate the natural development of bladder papilloma.
Methods or Approach:
A major dilemma in urological practice today is the inability of physicians to predict which benign-appearing papillomata will remain benign, recur, or ultimately invade. A sample of Baltimore-area urologists are participating in an investigation of all their patients with histological diagnosis of bladder papilloma. Biopsy and other tissue specimens are analyzed in a standard manner, urological and medical records are reviewed, and the patients interviewed concerning epidemiological risk factors including exposure to known and potential bladder carcinogens.
Results to Date:
Of a total of 183 papilloma patients, 63 (34.4 percent) have so far developed recurrent papillomas and 10 (5.5 percent) have developed bladder carcinoma. The papillary lesions associated with either subsequent recurrences or malignant transformation have not been readily distinguishable on the basis of histopathological characteristics of the lesions. However, cigarette smoking and occupational exposure to potential bladder carcinogens appear to be associated with malignant changes while relatively poorly predicting subsequent recurrences. An attempt is underway to develop a multivariate predictor for subsequent course which takes into account risk factors and histopathological characteristics as well as demographic and other confounding variables.
Project Dates:
1976–1986.
Financial Support:
University of Maryland Research Foundation.

1027. UNIVERSITY OF MARYLAND, SCHOOL OF MEDICINE, 660 West Redwood Street, Baltimore, Maryland 21201.

Project Title:
Pharmacology of Carcinogen Activation in Intact Cells.

Principal Investigator:
Kauffman, F.C.
Objective:
To delineate mechanisms whereby various nutritional factors and pharmacological agents influence the activation and

conjugation of precarcinogens in intact cells, using isolated perfused organs as experimental models.

Methods or Approach:

The influence of NADPH supply on rates of mixed-function oxidation in the isolated hemoglobin-free perfused rat liver and isolated hepatocytes will be investigated using benzo(*a*)pyrene, 7-ethoxycoumarin, and p-nitroanisole as model substrates. Alterations in rates of mixed-function oxidation that occur in the presence of specific inhibitors, inducing agents and alterations in nutritional status will be explored to determine the relative contribution of mitochondrial and cytosolic sources of NADPH and NADN. Steady-state concentrations of key intermediates of energy metabolism, pyridine nucleotides, and oxidation-reduction induced changes in surface fluorescence of intracellular pigments will be correlated with changes in rates of mixed-function oxidation and conjugation. The effect of altered nutritional status and selected inducing agents on rates of conjugation of the oxidized products of the model substrates will be studied in isolated perfused tissues. Rates of conjugation via various pathways will be compared with specific enzymes and measured concentrations of activated intermediates such as UDP glucuronic acid and PAPS to define rate-limiting factors for conjugation in intact tissues. An attempt will be made to enhance rates of conjugation of electrophiles generated from selected carcinogens in intact tissues. Factors regulating mixed-function oxidation and conjugation in perfused livers of various strains of mice known to differ in their susceptibility to chemical carcinogens will be explored. Continuing studies will involve DBA/2J and C57BL/6J mice, which are well characterized in terms of response to specific carcinogens and inducing agents. The influence of various nutritional factors and inducing agents on the microheterogeneity of enzymes associated with the formation of reduced cofactor, selected intermediates of energy metabolism and one or more components of the mixed-function oxidase system in liver will be explored using quantitative histochemical techniques.

Results to Date:

Project is in a preliminary phase.

Future Plans:

Factors influencing the transport of mutagenic conjugates from the liver will be examined.

Project Dates:

July 1976–June 1990.

Financial Support:

NCI (CA 20807).

1028. UNIVERSITY OF MARYLAND, Department of Agronomy, College Park, Maryland 20742.

Project Title:

Development of Low Alkaloid Maryland Tobacco.

Principal Investigators:

Aycock, M.K., Jr.; Mulchi, C.L.

Objective:

To develop breeding lines of Maryland air-cured tobacco that possess alkaloid (nicotine) levels between 0.2 and 0.5 percent by dry weight.

Methods or Approach:

A low-alkaloid burley 21 line (LA Bu 21) possessing total alkaloid levels of approximately 0.2 percent was crossed with Maryland 609, a popular cultivar of Maryland tobacco with alkaloid levels of approximately 2.0 to 2.5 percent. In the F_2 generation, a backcross program was initiated with Maryland 609 being used as the recurrent parent. Selection in each backcross and selfing generation is for low levels of total alkaloids. Alkaloid determination in each generation is made on dried plant tissue by steam distillation.

Results to Date:

The genetic material is segregating as predicted, and improvements are being observed with each successive backcross generation. Selection for the Maryland 609 plant type with a low alkaloid level is continuing. The fifth backcross was evaluated during the summer of 1984; low-alkaloid plants in this generation were selfed and will be evaluated during the summer of 1985. An additional backcross with Maryland 609 will be made in 1985.

Future Plans:

After a true-breeding, low-alkaloid Maryland 609 line has been developed, it will be evaluated for agronomic and chemical traits and comparisons will be made with the standard Maryland 609 cultivar.

Project Dates:

October 1974–December 1989.

Financial Support:

ARS, University of Maryland.

1029. UNIVERSITY OF MARYLAND, SCHOOL OF DENTISTRY, Department of Microbiology, Baltimore, Maryland 21201.

Project Title:

The Effect of Smokeless Tobacco Extracts on Oral Microorganisms Implicated in Periodontal Diseases and Cervical-Senile Caries.

Principal Investigator:

Falkler, W.A., Jr.

Objective:

To determine whether tobacco extracts inhibit or augment growth of microorganisms associated with oral diseases.

Methods or Approach:

Smokeless tobacco, when placed in the oral cavity, interacts with saliva; extracts of tobacco may have an effect on microorganisms that are present. Oral diseases of the age group that uses smokeless tobacco include marginal gingivitis, chronic periodontitis, acute necrotizing ulcerative gingivitis, and cervical-senile caries. These diseases have been associated with certain microorganisms. Active cultures of 26 strains of microorganisms implicated in periodontal diseases and cervical senile caries will be grown and an examination made of whether or not various concentrations of tobacco extracts have an influence on microorganism growth or serve as a substrate for growth.

Results to Date:

Smokeless tobacco extracts (10 mg/mL), when added to a basic salts solution, served as a growth substrate for the following oral microogranisms: (1) *Streptococcus mutans* (serotypes a through e); *S. salivarius* (13419); *S. sanguis* (167 N); *Actinomyces viscosus* (T14V); *Actinobacillus actinomycetemcomitans* (29522); *Bacteroides ochraceus* (27872); *Fusobacterium nucleatum* (10953); and *Veillonella parvula* (10790). However, *B. gingivalis* and *B. intermedius* did not grow. When smokeless tobacco extracts at a variety of concentrations were added to brain heart infusion medium (supplemented with hemin and menadione for the *Bacteroides* strains), all microorganisms grew. Smokeless tobacco extracts displayed no inhibitory activity.

Future Plans:

Attempts will be made to culture oral microorganisms from saliva before and after the use of smokeless tobacco to determine its effect on oral flora.

Project Dates:
January 1983–December 1985.
Financial Support:
Smokeless Tobacco Research Council, Inc.

1030. UNIVERSITY OF MARYLAND, Department of Agronomy, College Park, Maryland 20742.

Project Title:
Contamination of Maryland Tobacco by Heavy Metals From Sludge-Amended Soils.

Principal Investigators:
Mulchi, C.L.; Bell, P.
Objective:
To determine if heavy metals such as cadmium (Cd), lead (Pb), nickel (Ni), zinc (Zn), copper (Cu), and manganese (Mn), present in sludge, can be taken up by tobacco plants in quantities sufficient to contaminate the product and increase the health risk of smoking.
Methods or Approach:
Tobacco is known to be an accumulator of Cd, and smoking has been shown to be a primary source of Cd in the body. Tobacco was grown on soils that were amended with municipal sludge materials in the early 1970s. Rates of sludge application varied from 0 to 100 dry tons/acre, and sludge materials from different waste treatment plants were used. Data will be collected for 2 years from three growing areas on Cd, Zn, Cu, Mn, Pb, Ni, and iron (Fe) content of cured tobacco, using atomic absorption spectrophotometric techniques.
Results to Date:
At two sites in 1983, levels of all metals except Fe and Pb increased significantly with increasing sludge application rates of 0, 25, 50, and 100 tons/acre. Average contents by sludge application rates were Cd 3.9, 9.5, 12.7, and 16.4 μg/g; Ni 3.3, 2.9, 3.4, and 5.5 μg/g; Zn 53.0, 142.2, 246.2, and 445.1 μg/g; Cu 15.2, 29.0, 30.7, and 33.5 μg/g; Mn 115.4, 172.2, 209.3, and 442.5 μg/g; and Pb 2.5, 2.7, 2.8, and 2.9 μg/g. Fe rates were unchanged at 445.4, 395.2, 399.3, and 418.2 μg/g. Tobacco grown on soils with lower pH values had higher metal contents. The 1983 study was repeated in 1984 and the USDA site with multiple sludge sources, rates, and soil pHs was used.
Future Plans:
The 1984 studies will be repeated, and different tobacco cultivars will be grown on control soils and soils treated with high levels of sludge.
Project Dates:
January 1983–December 1986.
Financial Support:
ARS (58-3244-3-505); R.J. Reynolds Co. Inc.

1031. UNIVERSITY OF MARYLAND, SCHOOL OF MEDICINE, 655 West Lombard Street, Baltimore, Maryland 21201.

Project Title:
Factors Associated With Relapse Among Ex-Smokers.

Principal Investigator:
Wewers, M.E.
Objective:
To examine relationship between the relapse phenomenon and patient characteristics (social background and type of smoker); examine relationship with posttreatment characteristics (stressors, coping responses, family environment).
Methods or Approach:
To determine whether social background, type of smoker, stressors, coping responses, and family environment are efficient predictors of relapse, a one-group only, prospective design was utilized with 160 subjects enrolled in local smoking cessation clinics. The study volunteers were assessed prior to treatment for pretreatment smoking rate, particular smoking "type," based on Tomkins' typology, social background characteristics, and family environment. Three months after attending the clinic program, participants will be reassessed to determine posttreatment smoking rate, occurrence of stressors during the 3-month interval, and coping responses utilized to deal with not smoking.
Results to Date:
Project is in a preliminary phase.
Future Plans:
Based on study findings, smoking cessation interventions may be designed to include coping responses needed to deal with the presence of selected stressors, based on a person's social background, smoking type, and family environment factors.
Project Dates:
April 1984–September 1985.
Financial Support:
ALA.

1032. UNIVERSITY OF MARYLAND, Department of Bioscience, Catonsville, Maryland 21227.

Project Title:
Producing Safer Smoking Material by Reducing Tobacco Protein and Other Components.

Principal Investigator:
Kung, S.
Objective:
To study the feasibility of producing safer smoking material by reducing tobacco protein and related components.
Methods or Approach:
Biochemical and genetic studies will be conducted for reducing tobacco protein and related components, including use of plant hormones, controlled environmental conditions, and manipulation of genetic makeup. The tobacco gene coding for the large subunit of fraction 1 protein will be cloned and sequenced in order to regulate protein formation to achieve a safer tobacco.
Results to Date:
Five interspecific hybrids of tobacco were made (*N. sylvestris x N. glauca, N. sylvestris x N. plumbaginifolia, N. sylvestris X N. tomentosiformis, N. tabacum x N. glauca, and N. tabacum x N. glutinosa*). Interspecific hybrid plants were produced directly from F_1 seeds or by the clonal propagation from leaf tissue of a hybrid plant. Fraction 1 protein was crystallized from each hybrid plant and the kinetic properties of each hybrid enzyme were analyzed. The level of fraction 1 protein in relation to chlorophyll and dry weight in each hybrid is currently under investigation. The gene coding for the large subunit (LS) of fraction 1 protein is localized on chloroplast DNA (c-DNA). Therefore, ct-DNA from many species of *Nicotiana* has been isolated and purified. The LS gene has been cloned in *E. coli* and *B. subtilis* and a chloroplast genome library has been constructed. Attempts to regulate the expression of this gene in *B. subtilis* were also made.
Future Plans:
It is expected that some kind of regulation of this gene in vivo can be achieved.
Project Dates:
September 1980–April 1984.
Financial Support:
USDA (1090-20884-005S).
References:
Zhu, Y.S.; Duvall, E.J.; Lovett, P.S., et al. "*Nicotiana*

Chloroplast Genome: V. Construction, Mapping and Expression of Clone Library of *N. otophora* Chloroplast DNA." *Molecular and General Genetics* 1982. (2) Tasopoulou, D.; Kung, S.D. "*Nicotiana* Chloroplast Genome: IV. Evidence of Small Deletion and Repeated Sequence." *Theoretical and Applied Genetics*, 1982. (3) Zhu, Y.S.; Lovette, P.S.; Williams, D., et al. "Expression in *E. coli* and *B. subtilis* of Tobacco and *Chlamydomonas* Chloroplast DNA Sequences Coding for the Large Subunit of RuBP Carboxylase." *Nature*, 1983.

1033. USDA, ARS, BELTSVILLE AGRICULTURAL RESEARCH CENTER, Beltsville, Maryland 20705.

Project Title:
Improve Tobacco Safety by Biological Means.

Principal Investigators:
Skoog, H.A.; De Jong, D.W.; Spruill, W.M.

Objective:
To improve leaf safety of all tobacco types through biological means, including genetics, culture, selection, and breeding for desired chemical constituents, and botanical and physical characteristics, and for reduction of nicotine, tar, agriculture chemicals and other harmful constituents.

Methods or Approach:
Inheritance pattern of markers related to smoking and health will be established and plant variables that affect smoke components such as nicotine, tar and other undesirable components will be explored. Variables include plants with different genetic background, microfloral metabolites, planting density, fertilizer rate, and curing practice (e.g., formation of nitrosamines in relation to nitrogen fertilization). Germplasms will be screened for low tar, nicotine, and other characteristics. Plant varieties will be evaluated for stages of maturity for homogenized leaf curing and protein recovery and development of tissue and cell culture for obtaining safer tobacco material.

Results to Date:
Altering tobacco leaf chemical composition involves continued evaluation and modification of the tobacco germplasm collection. Selected genotypes in conjunction with foliar application of certain chemical growth enhancers that cause phase shifts in protein oscillation patterns were examined with regard to suitability for extraction and removal of leaf protein and lipid constituents that are suspected precursors of deleterious pyrolytic products formed during smoking. Evolutionary relationships between *Nicotiana* species were studied by restriction enzyme analysis of mitochondrial DNAs (mtDNA). Analysis of mtDNA indicated that the mitochondrial genome of *N. tabacum* is identical to that of *N. sylvestris*, which confirms that *N. sylvestris* is the maternal parent of *N. tabacum*. Examination of mtDNA of cytoplasmically male sterile (CMS) tobacco plants revealed differences in mtDNA between normal and CMS tobacco plants from the same species, showing the mitochondrial origin of certain CMS factors in tobacco. To avoid or lessen the use of chemicals for disease control, multiple disease resistance to several pathogens such as wildfire, angular leaf spot, and etch virus were advanced into breeding material.

Project Dates:
June 1979–December 1984.

Financial Support:
USDA (1208-20880-002D).

References:
De Jong, D.W. "Factors Related to Maximization of Protein Extraction From Green Leaves of Tobacco." In: Singh, N. (Editor). *Progress in Leaf Protein Research*. New Delhi, India, Today and Tomorrow's Printers and Publishers, 1983. (2) Cheng, A.L.S.; Skoog, H.A. "Water-Soluble Glycoproteins of Tobacco Leaves." *Journal of Agricultural Food Chemistry* 31:362-365, 1983. (3) Aycock, M.K., Jr.; Skoog, H.A.; Menchey, E.K., et al. "Performance of Maryland Varieties and Breeding Lines, 1981 and 1982." Maryland Agricultural Experimental Station Report, M.P. 985 (In press).

1034. USDA, ARS, BELTSVILLE AGRICULTURAL RESEARCH CENTER, Beltsville, Maryland 20705.

Project Title:
Improve Tobacco by Chemical and Physical Means.

Principal Investigators:
Tso, T.C.; Cheng, A.L.S.; Saunders, J.A.

Objective:
To identify chemical components and physical properties that are associated with leaf usability and smoking and health problems; modify or remove undesirable components to develop a safer tobacco by chemical and physical means.

Methods or Approach:
Chemical analysis and bioassay processes were used to isolate, identify, and characterize chemical components and physical properties related to leaf usability and smoking and health problems. Chemical, physical, and botanical markers were selected to establish a mathematical model of safer tobacco. Biosynthesis and distribution and metabolism of selected organic compounds during growth, senescence, and post-harvest handling were studied, and the source of inorganic components such as radioelements identified. Means for removal from harvested tobacco of precursors that contribute to smoke-related diseases were developed. All approaches involve growth of experimental tobacco, homogenized leaf curing, chemical extraction, physical treatment, reconstitution, smoke analysis, and bioassay.

Results to Date:
A procedure to extract nitrates from processed leaf material was developed. Tobacco–insect interactions were studied as a model system to investigate metabolism of toxins such as nicotine in tobacco. Biochemical characterizations of the enzymology of natural products, especially phenolics, will aid efforts to modify tobacco leaf chemistry. Recent investigations on the manipulation of tobacco protoplast membranes and electrofusion of protoplasts have the potential for allowing direct gene modification of the tobacco plant.

Project Dates:
June 1979–December 1984.

Financial Support:
USDA (1208-20880-001D).

References:
(1) Rhodes, P.R.; Saunders, J.A. "Selective Adsorption of Nitrate and Nitrite From Tobacco Leaf Homogenates." *Beitraege zur Tabakforschung International* 12(1):21-27, 1983. (2) Tso, T.C.; Kung, S.D. "Soluble Proteins in Tobacco and Their Potential Use." In: Telek, L., Graham, H.D. (Editors). *Leaf Protein Concentrates*. Westport, CT, AVI Publications Co., Inc., 1983, pp. 117-132. (3) Kosak-Channing, L.; Helz, G.R. "Solubility of Ozone in Aqueous Solutions of 0.06 M Ionic Strength at 5-30 C." *Environmental Science and Technology* 17(3):145-149, 1983. (4) Sisson, V.A.; Saunders, J.A. "Catalog of the Tobacco Introductions (*Nicotiana tabacum*). Supplement 1. Alkaloid Content of the Cured Leaf." *USDA Bulletin, Southern Series*, No. 27, 1983. (5) Olechno, J.D.; Saunders, J.A.; Conn, E.E. "Cinnamic Acid Hydroxylase Enzymes of Sorghum Bicolor, *Melilotus Alba*, and *Nicotiana*

Tabacum." Phytochemical Society of North America Newsletter 22:3, 1983.

1035. USDA, ARS, UNIVERSITY OF MARYLAND, College Park, Maryland 20742.

Project Title:
Homogenized Leaf Curing of Maryland Tobacco.

Principal Investigator:
McKee, C.
Objective:
To develop and perfect a method of homogenized leaf curing (HLC) on Maryland tobacco, coupled with removal of soluble proteins, polyphenols, nitrate, and possible radio-elements.
Methods or Approach:
The stability of soluble proteins was investigated under various conditions after harvesting with or without homogenizations; enzymatic activities during incubation were examined and various drying processes to achieve protein recovery and desirable tobacco material were evaluated. A laboratory procedure that involves binding of nitrate to PVB nitron, which is linked to sand to enable recovery of nitrate, was developed for removal of excess nitrate in soluble fractions of freshly ground tobacco. Nitrate in leaf tobacco may serve as precursor for undesirable smoke compounds, including NO_x, HCN, quinoline, and possibly nitrosamine.
Results to Date:
In a pilot test, approximately 400 lbs of fresh weight Maryland 872 tobacco was processed at the HLC plant at Oxford, N.C. PVB nitron-coated sand seems to work well for removing nirate from homogenized tobacco leaves. If PVB nitron had been applied to the sand in sufficient quantity to saturate the system, it would have taken only 10 kg rather than 50 kg of sand to conduct the bulk experiment.
Project Dates:
June 1979–February 1983.
Financial Support:
USDA (1090-20881-002S).
Reference:
Rhodes, P.R.; Saunders, J.A. "Selective Adsorption of Nitrate and Nitrite From Tobacco Leaf Homogenates." *Beitraege zur Tabakforschung*(In press).

1036. VETERANS ADMINISTRATION MEDICAL CENTER, 3900 Loch Raven Boulevard, Baltimore, Maryland 21218.

Project Title:
The Electrophysiologic Effect of Cigarette Smoke.

Principal Investigator:
Peters, R.W.
Objective:
To examine the electrophysiologic effects of smoking in patients undergoing cardiac catheterization for routine diagnostic reasons.
Methods or Approach:
All subjects will be inpatients who are smokers and are undergoing diagnostic cardiac catheterization and coronary arteriography. The electrode catheter used for atrial pacing during coronary arteriography will be left in the right atrium and used for atrial pacing and recording during the research protocol. Using local anesthesia, an additional electrode catheter will be inserted percutaneously into the right femoral vein and advanced to the area of the tricuspid valve for the purpose of recording the His bundle electrogram. After recording initial conduction times, atrial pacing will be initiated at a paced cycle length 50 msec below the spontaneous cycle length and conduction times and sinus node recovery times will be determined at 50 msec increments up to a paced cycle length of 300 msec (200 beats/min). Pacing will be done for 60 seconds at rates below 150 beats/min and for 15-30 seconds at rates of 150 beats/min and above. Conduction system refractory periods will then be determined using programmed premature stimuli during continuous atrial pacing at a rate of 100 beats/min. The high light atrial catheter will then be positioned in the apex of the right ventricle and pacing and programmed stimulation will be repeated, using an identical protocol, from the right ventricle. Vital signs will be carefully monitored and the procedure will be immediately terminated if any adverse effects occur. Two standard cigarettes will then be smoked in rapid succession and overdrive pacing and programmed premature stimulation from the right atrium and ventricle will be repeated. The procedure should last approximately 40 min and fluoroscopy time should be about 5 min. If the post-pacing lasts longer than 20 min, one additional cigarette will be smoked to assure maintenance of an adequate blood nicotine concentration.
Results to Date:
A total of five patients have been studied under this protocol to date. No adverse effects have been seen.
Financial Support:
VA.

1037. BAYSTATE MEDICAL CENTER, Wesson Memorial Unit, 140 High Street, Springfield, Massachusetts 01105.

Project Title:
Quantitative Correlation of Lifetime Tobacco Consumption.

Principal Investigator:
Turner, J.W.

Objective:
To (1) test the validity of quantity of tobacco consumed and rate of development of different diseases; (2) utilize the information obtained for professional and lay education on tobacco-related disease; (3) develop a workable questionnaire on tobacco use for patient interviews to be used routinely as a clinical tool; (4) develop nuclear imaging techniques for study of patients with lung cancer and emphysema, correlated with lifetime tobacco exposure; and (5) develop thermographic techniques to assess peripheral vasoconstriction related to smoking.

Methods or Approach:
Several generations of tobacco questionnaires for interview of patients on admission have been developed. This information is correlated with admission chest X-ray study and with varied diseases identified during corresponding hospital stays. Lung cancer has been of primary interest, but additional assessment has been made of chronic obstructive pulmonary disease, cardiovascular disorders, and cancers of the urinary bladder in the same patients.

Results to Date:
Project has resulted in a 90-minute instruction course entitled "The Role of the Radiologist in Tobacco Use Diseases" presented in 1968, a two-part videotape production on malignant and nonmalignant aspects of tobacco-related diseases among general hospital patients, and other instructional materials on smoking and disease.

Future Plans:
Efforts will be continued to educate the medical profession on the size of the tobacco disease problem and on the practicality of determining as precisely as possible total lifetime consumption of cigarettes, cigars, pipe smoking, and snuff use by a quantitative approach. A segment of the study (which involved smokers who had consumed more than one-half million cigarettes) was presented at the World Cancer Congress XIII, Seattle, Washington, September 1982.

Project Dates:
July 1950–July 1985.

Financial Support:
Baystate Medical Center.

1038. BOSTON CITY HOSPITAL, 818 Harrison Avenue, Boston, Massachusetts 02118.

Project Title:
Maternal Marijuana Use and Pregnancy Outcome.

Principal Investigators:
Zuckerman, B.S.; Sorenson, J.

Objective:
To examine whether maternal marijuana use during pregnancy is associated with poor pregnancy and neonatal outcomes when other adverse interrelated maternal habits and characteristics are controlled analytically; assess impact of urine testing on reporting of use of certain substances such as cigarettes, marijuana, alcohol, and cocaine in pregnancy.

Methods or Approach:
Pregnant women receiving prenatal care at Boston City Hospital will be evaluated at initial prenatal interview (T1), during the third trimester (T2), and following delivery (T3). Detailed interviews, medical record audits, and anthropometric measures of the 1,500 women will be used to determine health, nutritional status, health habits, and psychoactive drug use during each trimester. In addition, urine assays will assess presence of marijuana and cocaine. Women are randomly assigned to one of two groups: (1) women who will have urine tested for presence of marijuana and nicotine and asked to report on drug use; and (2) women who will be asked about drug use without urine assays. Comparisons of self-report between the two groups will be conducted.

Results to Date:
Results are not yet available.

Project Dates:
March 1984–February 1988.

Financial Support:
NIDA (1R01DA03508).

1039. BOSTON UNIVERSITY MEDICAL CENTER, Drug Epidemiology Unit, 1371 Beacon Street, Brookline, Massachusetts 02146.

Project Title:
Multiple Case–Control Study of the Long Term Effects of Drug Use in the Treatment of Chronic Disease.

Principal Investigators:
Shapiro, S.; Rosenberg, L.; Kaufman, D.

Objective:
To identify diseases requiring hospitalization that are caused by environmental factors such as drugs, cigarette smoking, alcohol consumption, coffee drinking, and saccharin use.

Methods or Approach:
Full-time nurse interviewers, stationed in selected hospitals throughout the United States, interview patients concerning lifetime medication exposure, habits such as smoking and coffee drinking, and relevant medical histories to obtain covariates of interest. Information is checked and coded in a central facility, stored on computer, and subjected initially to frequent analysis for screening purposes and, if necessary, to more detailed analysis.

Results to Date:
A correlation has been found between cigarette smoking and increased risk for myocardial infarct in women under age 50 who are otherwise in good health; the correlation also exists in predisposed women. The effect of age and predisposition on this association has been evaluated. Also, the increase in the risk of myocardial infarct among women who use oral contraceptives was found to be greatly enhanced among heavy smokers. Natural menopause occurs earlier in smokers than in women who do not smoke. The risk of breast cancer does not appear to be influenced by cigarette smoking.

Future Plans:
The data file, which currently consists of approximately 50,000 patients, will continue to be a resource for the generation and testing of hypotheses concerning environmental factors such as drugs, cigarette smoking, and disease.

Project Dates:
July 1976–continuing.

Financial Support:
FDA (U01FD01222-03); NICHD (N01HD22820).

References:
(1) Rosenberg, L.; Miller, D.R.; Kaufman, D.W., et al. "Myocardial Infarction in Women Under 50 Years of Age." *Journal of the American Medical Association* 250:2801-2806, 1983. (2) Rosenberg, L.; Schwingl, P.J.; Kaufman, D.W., et al. "Breast Cancer and Cigarette Smoking." *New England Journal of Medicine* 310:92-94, 1984.

1040. BOSTON UNIVERSITY MEDICAL CENTER, Drug Epidemiology Unit, 1371 Beacon Street, Brookline, Massachusetts 01246.

Project Title:
Myocardial Infarction in Young Men in Relation to Vasectomy.

Principal Investigators:
Shapiro, S.; Rosenberg, L.
Objective:
To determine whether vasectomy in young men is associated with subsequent increased risk of nonfatal myocardial infarction (MI); examine other risk factors for MI in young men.
Methods or Approach:
Cases of acute first episode MI in men under 55 years of age were ascertained by weekly telephone calls to coronary care units of 78 collaborating hospitals in eastern Massachusetts and southern Connecticut. Locally stationed nurse-interviewers interviewed cases and hospital controls to obtain data on general characteristics, history of vasectomy, smoking history, and presence of other risk factors for MI. Effects of risk factors were evaluated individually and in various combinations.
Results to Date:
There is a strong relationship between the number of cigarettes smoked and risk of MI, but no relationship was found between tar and nicotine content of cigarettes and risk. Alcohol consumption did not appear to influence risk of MI. Data analysis will continue.
Project Dates:
April 1980–October 1983.
Financial Support:
NICHD (N01HD02810).
References:
(1) Kaufman, D.W.; Helmrich, S.P.; Miettinen, O.S., et al. "Nicotine and Carbon Monoxide Content of Cigarette Smoke and the Risk of Myocardial Infarction in Young Men." *New England Journal of Medicine* 308:409-413, 1983. (2) Kaufman, D.W.; Rosenberg, L.; Helmrish, S.P., et al. "Alcoholic Beverages and Myocardial Infarction in Young Men." *American Journal of Epidemiology* (In press).

1041. BOSTON UNIVERSITY, SCHOOL OF MEDICINE, THE FRAMINGHAM HEART STUDY, 118 Lincoln Street, Framingham, Massachusetts 01701.

Project Title:
The Framingham Offspring Study (Cycle III).

Principal Investigator:
Stokes, J., III.
Objective:
To (1) study approximately 4,000 subjects previously enlisted in the Framingham Offspring Study (Cycle I) initiated in 1971; (2) assess cardiovascular function, cardiac structure, personal habits, and general physical condition; (3) provide necessary information about incidence, precursors, and etiology of subclinical endpoints that are becoming indicators for drug therapy and other kinds of intervention; and (4) provide better identification of a profile for high risk of cardiovascular disease.
Methods or Approach:
All examinations are performed at the Framingham Heart Study Clinic; however, ancillary studies will be conducted at the Framingham Union Hospital (laboratory determinations), Department of Health Sciences at Sargent College of Boston University, Northeastern Region Human Nutrition Research Center on Aging at Tufts University, Endocrine-Diabetes Section of the Tufts Medical Service at the Veterans Administration Medical Center in Boston, Department of Physiology and Biophysics at Harvard Medical School, and the American Institutes for Research and Behavioral Sciences in Cambridge, Massachusetts.
Results to Date:
Results are not yet available.
Project Dates:
1983–1986.
Financial Support:
NHLBI (N01HV38038).

1042. BOSTON UNIVERSITY, SCHOOL OF MEDICINE, Department of Pathology, 80 East Concord Street, Boston, Massachusetts 02118.

Project Title:
Student Evaluation of the Impact of Group Health Education on Cigarette Smoking.

Principal Investigator:
Reif, A.E.
Objective:
To evaluate the impact of assemblies concerning health effects of smoking in adolescents.
Methods or Approach:
Assemblies on the medical effects of cigarette smoking are given to groups of 100-350 adolescents, usually in grades 6 (12-year-olds), 7 (13-year-olds), and 8 (14-year-olds). Between 4 and 12 weeks after the assembly, the students are given a 24-question evaluation sheet (questionnaire) on which they are asked to note their reaction to the assembly, their smoking habits prior to the assembly, and any change that occurred in their smoking habits following the assembly. Their reasons for taking up smoking (if they smoke) or for disliking smoking (if they don't smoke) are also required.
Results to Date:
Approximately 40 percent of the students who said they smoked before the assembly had quit immediately after the assembly. By the time the questionnaire was taken, roughly one-third of those who had quit had started to smoke again.

1043. BOSTON UNIVERSITY, MEDICAL CENTER, Drug Epidemiology Unit, 777 Concord Avenue, Cambridge, Massachusetts 02138.

Project Title:
Birth Defects Interview Study.

Principal Investigator:
Mitchell, A.A.
Objective:
To continue an ongoing investigation of the relationship between environmental factors during pregnancy (such as drugs and cigarette smoking) and birth defects in the offspring.
Methods or Approach:
This is a case–control study involving three metropolitan areas (Boston, Philadelphia, and Toronto, Canada) and part of the State of Iowa. Nurse-interviewers identify infants with malfor-

mations from participating centers and conduct standard home interviews of the parents within 6 months of the birth. Information is obtained on family characteristics and medical risk factors. Detailed histories of drug exposure, cigarette smoking, and other environmental factors are also elicited. The information is checked, coded, stored on computer, and subjected to frequent screening and ad hoc analyses.

Results to Date:
To date, information on 5,500 malformed infants has been obtained. The relationship between cigarette smoking and birth defects is being evaluated, with attention to the possible interaction with caffeinated beverages.

Future Plans:
It is hoped that the study can be expanded to become a national resource for the generation and testing of hypotheses concerning environmental factors, including drugs and cigarette smoking, and birth defects.

Project Dates:
July 1975–continuing.

Financial Support:
Hoffmann-La Roche; FDA; Merrell-Dow; NICHD (HD 22820).

1044. BOSTON UNIVERSITY, SCHOOL OF MEDICINE, 80 East Concord Street, Boston, Massachusetts 02118.

Project Title:
Elastase Versus an Anti-Elastase in the Genesis of Emphysema.

Principal Investigators:
Snider, G.L.; Franzblau, C.; Stone, P.J., et al.

Objective:
To investigate the role of balance of elastase and antielastase in the pathogenesis of emphysema using animal model systems and investigations in humans.

Methods or Approach:
A variety of techniques are being used to explore the role of human neutrophil elastase in the genesis of emphysema in hamsters, and its interaction with naturally occurring and synthetic antiproteases. Functional antiprotease levels are being evaluated in bronchoalveolar lavage fluid and blood of smokers with and without airflow obstruction. The interaction of human neutrophil elastase with human alveolar macrophages is being explored.

Results to Date:
Data collection is continuing.

Project Dates:
1972–continuing.

Financial Support:
NHLBI (19717).

1045. BOSTON UNIVERSITY, One Boylston Plaza, Prudential Center, Boston, Massachusetts 02199.

Project Title:
Support for Clinical Center for Heart Disease.

Principal Investigator:
Thomas, H.E.

Objective:
To determine current status of risk factors for 700 men who participated in a multiple risk factor intervention trial, 3 years after completion of the trial.

Methods or Approach:
A followup screening of original participants is being carried out to determine changes in risk factor status. Factors that determine success or failure in maintaining risk factor change are being evaluated.

Results to Date:
Results are not yet available.

Financial Support:
NHLBI (3N01HV33106-14).

1046. BOSTON UNIVERSITY, SCHOOL OF MEDICINE, Veterans Administration Outpatient Clinic, 17 Court Street, Boston, Massachusetts 02108.

Project Title:
Normative Aging Study.

Principal Investigators:
Vokonas, P.S.; Bosse, R.; Borkan, G.A., et al.

Objective:
To investigate longitudinal age changes in selected male subjects.

Methods or Approach:
Since its inception in 1963, the Normative Aging Study (NAS) has been primarily involved with collection, storage, and analysis of data on over 7,500 variables from more than 2,000 initially healthy male volunteers. Areas of investigation include (1) clinical medicine (cardiovascular and pulmonary function, biochemical studies, clinical pathology); (2) special senses (audiology and ophthamology); (3) anthropometry and body composition; and (4) psychosocial studies (personality, memory, smoking habits, drinking behavior, work, retirement). In addition, independent dental and behavioral studies have evolved that operate in close collaboration with the NAS. Aspects of smoking studies include (1) effect of age and smoking on pulmonary function, body composition, blood pressure, hormonal, platelet, and immunologic function, and incidence of cardiovascular disease; (2) smoking and psychosocial stress (addictive behavior, anxiety, neuroticism, and extroversion); and (3) smoking cessation (methods, secular trends, weight change following cessation, and factors related to recidivism).

Results to Date:
Analysis of secular trends in smoking behavior from 1962 to 1975 shows an increase in cessation rates during the late 1960s followed by a leveling off of cessation in the early 1970s. Incidence of coronary heart disease was more closely related to changes in serum cholesterol and triglycerides over time than to initial levels. Electrocardiographic findings suggestive of left ventricular hypertrophy can help predict subsequent development of hypertension. Hypertension is also related to significant differences in regional body fat distribution.

Project Dates:
1963–continuing.

Financial Support:
VA; NIA; NCI; NHLBI; NIAAA.

References:
(1) Baden, L.; Weiss, S.T.; Thomas, H.E., Jr., et al. "Smoking Status and the Electrocardiogram: A Cross-Sectional and Longitudinal Study" *Archives of Environmental Health* 37:365-369, 1982. (2) Chao, F.C.; Tullis, J.L.; Alper, C.A., et al. "Alteration in Plasma Proteins and Platelet Functions With Aging and Cigarette Smoking in Healthy Men." *Thrombosis and Haemostatis* 41:259-264, 1982. (3) Garvey, A.J.; Bosse, R.; Glynn, R.J., et al. "Smoking Cessation in a Prospective Study of Healthy Adult Males: Effects of Age, Time Period, and Amount Smoked." *American Journal of Public Health* 13:446-450, 1983. (4) Heinoid, J.W.; Garvey, A.J.; Goldie, C.L., et al. "Retrospective Analysis in Smoking Cessation Research." *Addictive Behaviors* 7:347-353, 1982. (5) Sparrow, D.; Beauso-

leil, N.E.: Garvey, A.J., et al. "A Cross-Sectional and Longitudinal Analysis of the Influence of Cigarette Smoking and Age on Bone Loss in Men." *Archives of Environmental Health* 37:246-249, 1982. (6) Sparrow, D.; Stefos, T.; Bosse, R., et al. "The Relationship of Tar Content to Decline in Pulmonary Function Among Cigarette Smokers." *American Review of Respiratory Disease* 127:56-58, 1983. (7) Bosse, R.; Rose, C.L. (Editors). *Smoking and Aging*. Lexington, Massachusetts, Lexington Books, 1984. (8) Sparrow, D.; Glynn, R.J.; Cohen, M., et al. "The Relationships of the Peripheral Leukocyte Count and Cigarette Smoking to Pulmonary Function Among Adult Men." *Chest* 86:383-386, 1984.

1047. BOSTON UNIVERSITY, HEALTH POLICY INSTITUTE, 53 Bay State Road, Boston, Massachusetts 02215.

Project Title:
Legal Approaches That Encourage the Reduction of Smoking. Corporate Smoking Policies: How Far Can They Go?

Principal Investigator:
Walsh, D.C.

Objective:
To (1) review, critique, and synthesize available literature and catalog existing legal approaches in the United States to the smoking problem; (2) summarize what is currently known about how effective approaches are in encouraging smoking reduction; (3) identify areas needing more research and areas where it is time to act; (4) understand the process through which corporations decide to implement smoking policies; (5) identify specific aspects of the policies that may be more or less difficult to shepherd through the corporation; (6) examine the force field within which policies are debated (who supports and who challenges them); (7) identify arguments that are marshalled; and (8) elucidate stages through which the proposed policies pass on their way to adoption.

Methods or Approach:
The project is chiefly a literature and document review. Exploratory interviews will also be conducted, followed by a proposed national level working conference.

Results to Date:
Results are being prepared for, or are already in publication.

Project Dates:
December 1982–continuing.

Financial Support:
NSF; Center for Industry and Health Care.

Reference:
Walsh, D.C. "Corporate Smoking Policies: A Review and An Analysis." *Journal of Occupational Medicine* 26(1):17-22, 1984.

1048. BOSTON UNIVERSITY, SCHOOL OF MEDICINE, 80 East Concord Street, Boston, Massachusetts 02118.

Project Title:
Induction of Emphysema by Human Neutrophil Elastase.

Principal Investigator:
Stone, P.J.

Objective:
To determine role of human neutrophil elastase (HNE) in genesis of human emphysema; develop methods for prevention.

Methods or Approach:
Induction of emphysema will be studied by instilling HNE into the lungs of hamsters. Using biochemical, morphometric, histologic, and physiologic approaches, HNE-induced emphysema lesions will be characterized by defining dose–response behavior, progression with time, and fate of instilled ^{125}I-HNE. Investigations will include different in vivo tissue responses to HNE and porcine pancreatic elastase (PPE), and preferential binding to HNE by α_1-protease inhibitor (α_1PI) that inactivates HNE, in contrast to preferential binding of PPE by α_2-macroglobulin, which protects elastolytic potential of the enzyme. The hypothesis that differences between HNE and PPE in preferences for different parts of the lung as a substrate may play a role will be tested. Determination will be made as to whether human neutrophil myeloperoxidase or α_2-macroglobulin-HNE potentiate HNE-induced lesion, using ^{125}I-HNE as a marker. The possible mediating role of hamster alveolar macrophages in pathogenesis will be assessed. Moderation of HBE-induced emphysema by synthetic and naturally occurring inhibitors will be correlated with in vitro parameters of inhibition to facilitate development of more effective synthetic antielastases.

Results to Date:
In studies of α_1PI, findings failed to show a relationship between cigarette smoking and levels of functionally active α_1PI in the lower respiratory tract of smokers. Smokers did not have less functionally active α_1PI (capable of inhibiting elastase) in lung lavage fluid or plasma than nonsmokers. An unsuccessful attempt was made to raise the level of functional α_1PI in smokers' lavage fluid by using reducing conditions that have been reported to restore functional activity of oxidized α_1PI. Although the possibility that cigarette smoke may damage α_1PI in microenvironments in the lower respiratory tract of smokers was not excluded, the high level of neutrophils in smokers' lungs is a rich source of elastase and oxidants of α_1PI, and seems likely to be a reason for localized perturbation of the elastase–antielastase balance and development of emphysema. To facilitate development of elastase inhibitors that might be used therapeutically, a number of agents were tested. Although oligopeptide chloromethyl ketone compounds are toxic, it was shown that pretreatment of hamsters with these agents moderates HNE-induced emphysema. More potent and less toxic agents are currently being tested. Preliminary data indicate a good correlation between the I.C.$_{50}$ (concentration of inhibitor required for 50 percent inhibition of elastolytic activity) of various agents and the ability to moderate HNE-induced lesion in the hamster.

Project Dates:
December 1982–December 1985.

Financial Support:
NHLBI (HL 25229).

1049. BRANDEIS UNIVERSITY, Department of Biochemistry, Waltham, Massachusetts 02254.

Project Title:
Nicotine and Tobacco Compounds: Metabolic Consequences.

Principal Investigator:
Van Vunakis, H.

Objective:
To (1) study metabolism of nicotine and related derivatives to better understand enzyme systems involved; (2) analyze for nicotine and cotinine in blood, urine, saliva, and other experimental samples obtained from subjects participating in epidemiological studies; (3) determine relationship between nicotine and/or cotinine levels and behavioral patterns and reported smoking habits; (4) determine whether nicotine and cotinine levels are better predictors of diseases attributed to smoking than other biochemical indicators or verbal testimony; (5) sensitize radioimmunoassays for nicotine and cotinine

to detect levels in passive smokers and during postdistributive phase of nicotine intake when levels of the alkaloids can be quite low; and (6) determine effect of concomitant drug intake on nicotine metabolism.

Methods or Approach:
Nicotine and its metabolites (or suitable derivatives) are covalently linked to macromolecules for immunization of experimental animals. Antibodies produced in this way have been used to develop specific radioimmunoassays that are capable of detecting picomolar quantities of individual compounds in experimental samples. Hybridoma technology will be used to obtain stereospecific antibodies.

Results to Date:
Compared with other methods of analysis, radioimmunoassays appear to be the method of choice where a large number of samples must be analyzed. Among indicators commonly used to detect nicotine exposure, cotinine is proving to be the most reliable, since it is a metabolic product of nicotine and originates only from that source. Various steroids were tested for ability to inhibit nicotine to cotinine conversion. Norethisterone and ethynylestradiol, which contain a 17-acetylenic function and are known to covalently bind to the heme moiety of cytochrome P-450, were found to be powerful inhibitors of this reaction. In vitro findings may have physiological implications, since studies that link use of oral contraceptives and smoking with a higher risk of cardiovascular disease have been reported. More research is required to evaluate physiological implications of the in vitro study in relation to epidemiological findings.

Future Plans:
Hybridoma technology will be used to obtain monoclonal stereospecific antibodies for (-)nicotine, (+)nicotine, (-)cotinine, and (+)cotinine. Antibodies will be characterized and used to sensitize immunoassays for (-)nicotine and (-)cotinine. Plasma samples from human subjects will be analyzed for cotinine to determine differences in levels between smokers who utilize other drugs and smokers who are drug free (particularly women who do or do not use oral contraceptives containing 17-ethynyl sterols).

Project Dates:
January 1985–January 1988.

Financial Support:
NIDA (5R02DA02507).

1050. BRANDEIS UNIVERSITY, Department of Biochemistry, 415 South Street, Waltham, Massachusetts 02254.

Project Title:
Purification and Properties of a Soluble NAD(P) Glycohydrolase Isolated From the Sponge *M. Prolifera*.

Principal Investigator:
Van Vunakis, H.

Objective:
To investigate the existence of NAD(P) glycohydrolase (in sponges) that has properties that make it an ideal candidate for mechanistic and structural studies required to understand its catalytic activities.

Methods or Approach:
It has previously been shown that NAD(P) glycohydrolase from some mammalian sources can catalyze the exchanges of nicotine and cotinine for the nicotinamide moiety of the coenzyme. Analogs of nicotine and cotinine have been prepared and immunoassays and chromatographic methods have been developed for isolation and quantification. Analogs have been detected in rabbits receiving nicotine and in autopsy tissue of smokers, but not in similar tissue obtained from nonsmokers. Experiments will be conducted to (1) purify NAD(P) glycohydrolase to homogeneity and determine some of its physical and chemical properties; (2) determine dependence of glycohydrolase and transferase reactions on environmental factors; (3) determine some kinetic parameters for glycohydrolase reaction and for transglycosidation reaction, using acetylpyridine, nicotine, and cotinine as substrates; and (4) immunize animals with the enzyme to obtain antibodies that can be used to develop immunoassays to detect and quantify the enzyme and to determine extent of cross-reactivity with similar enzymes from other species. It is anticipated that an indication of the evolutionary development of the class of enzymes may be found.

Results to Date:
Soluble NAD(P) glycohydrolase from the sponge *M. prolifera* has been purified to apparent homogeneity by procedures based on the principles of ion exchange, affinity, and gel permeation chromatography. Electrophoresis revealed the presence of one protein band when gels were developed by silver staining. Antisera obtained from rabbits immunized with the purified enzyme gave a single band of precipitation with the homologous antigen in Ouchterlony double diffusion plates. Amino acid analysis after acid hydrolysis showed a preponderance of acidic amino acids. The properties of the enzyme on the ion exchange resins is also consistent with its being an acidic protein. It may contain carbohydrate moieties that contribute to its overall charge.

Future Plans:
Sufficient quantities of purified enzyme will be prepared for studies on its chemical properties and attempts to elucidate mechanisms of action.

Project Dates:
July 1984–July 1985.

Financial Support:
CTR.

1051. BRIGHAM AND WOMEN'S HOSPITAL, 75 Francis Street, Boston, Massachusetts 02115.

Project Title:
Association of *Ureaplasma urealyticum* in the Placenta With Perinatal Morbidity and Mortality.

Principal Investigators:
Kundsin, R.B.; Driscoll, S.G.; Monson, R.R., et al.

Objective:
To investigate presence of ureaplasmas, mycoplasmas, chlamydiae, fungi, aerobic and anaerobic bacteria, and cytomegalovirus in fetal membranes; evaluate association with perinatal morbidity and mortality.

Methods or Approach:
Placentas from three groups of subjects were cultured: 144 who died in the perinatal period, 452 neonates admitted to the intensive care unit, and 205 controls. Information on smoking was available for only 319 subjects included in the previous interview study.

Results to Date:
When current cigarette smoking was included in the model with other factors, and when the study was limited to the 278 women with membrane-rupture intervals of less than 48 hours, the odds ratio for the association between low birth weight and *U. urealyticum* was 2.1 (1.1 to 4.2) and for cigarette smoking 1.6 (0.9 to 3.0). Smoking was positively related to colonization of *U. urealyticum*. Gestational age and birth weight were inversely related to isolation of ureaplasma and chorioamnionitis was positively related to isolation. The presence of ureaplas-

mas in the placenta suggests transcervical migration of microorganisms from the lower genitourinary tract. Data show a strong association between ureaplasma infection of the placenta and low birth weight and suggest that the association is causal.

Financial Support:
NICHHD (HD-10984).

Reference:
Kundsin, R.B.; Driscoll, S.G.; Monson, R.R., et al. "Association of *Ureaplasma urealyticum* in the Placenta With Perinatal Morbidity and Mortality." *New England Journal of Medicine* 310:941-945, April 12, 1984.

1052. CHILDREN'S HOSPITAL MEDICAL CENTER, 300 Longwood Avenue, Boston, Massachusetts 02115. BOSTON UNIVERSITY, MEDICAL CENTER, Drug Epidemiology Unit, 777 Concord Avenue, Cambridge, Massachusetts 02138.

Project Title:
Pediatric Intensive Drug Surveillance Program (PeDS).

Principal Investigator:
Mitchell, A.A.

Objective:
To identify and quantify the clinical effects of drugs in hospitalized children, with particular emphasis on unsuspected adverse effects.

Methods or Approach:
In this intensive drug surveillance program, full-time monitors are stationed on selected pediatric wards, where they obtain information on medications given to patients and on various adverse occurrences taking place during the period of hospitalization. The information is checked and coded, stored on computer, and subjected to frequent screenings and analyses to quantify known effects as well as to identify unsuspected ones. Information on a wide variety of factors, including smoking habits, is obtained on both the patient and his or her parents.

Results to Date:
Project is in a preliminary phase.

Future Plans:
It is hoped that this data file, which currently contains data on over 8,500 patients, will be expanded and become a national resource for both the generation and testing of hypotheses concerning adverse clinical occurrences in relation to environmental factors such as drugs and smoking.

Project Dates:
July 1974–January 1987.

Financial Support:
FDA (22380-3001); HRSA (MCJ 250484); NICHD (HD 17958).

1053. HARVARD MEDICAL SCHOOL, BRIGHAM AND WOMEN'S HOSPITAL, Channing Laboratory, 180 Longwood Avenue, Boston, Massachusetts 02115.

Project Title:
Risk Factors for Myocardial Infarction in Women.

Principal Investigators:
Hennekens, C.H.; Willett, W.; Rosner, B., et al.

Objective:
To utilize data from an existing cohort of 120,000 women, aged 30 to 55 in 1976, to study risk factors for myocardial infarction in women.

Methods or Approach:
Exposures to oral contraceptives, postmenopausal estrogens, and cigarette smoking have been documented, as have menopausal status, a past history of hypertension, diabetes, angina pectoris, and hypercholesterolemia, and family history of myocardial infarction. Retrospective data have been collected for the period prior to 1976, and prospective data, including dietary practices, were collected biennially through 1982. Information is gathered by mail questionnaires, with further documentation of events by review of hospital records. Simple, stratified, and multivariate analyses will all be employed to elucidate the separate relationships of the risk factors with myocardial infarction in women, in both retrospective and prospective data. Interactive effects will be emphasized in both data sets.

Results to Date:
Among 249 women with nonfatal myocardial infarction (MI) and 4,977 controls matched on the basis of age, smokers experienced a threefold increase in risk of MI relative to nonsmokers, which was not explained by hypertension, diabetes, high cholesterol, or familial MI. Women who had stopped smoking did not exhibit any increased risk. In comparing smoking and oral contraceptive (OC) use, among 156 premenopausal women with nonfatal MI and 3,120 controls matched on age and menopausal status, current OC use increased risk of MI, and the combined effects of OC use, smoking, and hypertension were synergistic.

Future Plans:
Further analyses will explore relationships of hormones and diet with coronary heart disease in women, risk factors for pulmonary embolism, angina pectoris, and cerebrovascular disease in women, and risks of coronary disease associated with smoking various types of cigarettes in women.

Project Dates:
August 1980–1983.

Financial Support:
NHLBI (HL 24074).

1054. HARVARD MEDICAL SCHOOL, BRIGHAM AND WOMEN'S HOSPITAL, Channing Laboratory, 180 Longwood Avenue, Boston, Massachusetts 02115.

Project Title:
Risk Factors for Cardiovascular Disease in Women.

Principal Investigators:
Hennekens, C.H.; Stampfer, M.; Rosner, B., et al.

Objective:
To examine and quantify the interrelationships of cigarette smoking with hormonal factors, a variety of nutrients, and subsequent risk of coronary heart disease, pulmonary embolism, angina pectoris, and stroke in a cohort of 121,964 female registered nurses aged 30 to 55 years in 1976.

Methods or Approach:
The cohort was established in 1976 and information is gathered by mailed questionnaire every 2 years. In addition to cigarette smoking history and brand smoked, exposures include use of postmenopausal hormones, diet, physical activity, medication use, family history, and a number of other risk factors. Incident cases of nonfatal myocardial infarct (MI), pulmonary embolism, angina pectoris, stroke, and peripheral venous thrombosis are also ascertained. Fatal cardiovascular events are identified through reports of family members and death searches for nonrespondents, using the National Death Index. All diagnoses are documented through review of medical records.

Results to Date:
Prospective data from 1976–1978, analyzed for the association

between smoking and nonfatal MI, shows that the age-adjusted relative risk among current smokers was 7.9 compared with never smokers. Risk of MI among smokers of 1 to 14, 15 to 24, and >25 cigarettes/day were 3.5, 7.6, and 10.7, respectively, compared with never smokers. Data for 66,663 nurses who were premenopausal in 1976 showed that smoking and low relative weight were independently associated with higher rates of menopause, although the effect of weight was almost exclusively confined to smokers.

Future Plans:
Future analyses will explore other interrelationships noted in objectives.

Project Dates:
December 1980–November 1987.

Financial Support:
NHLBI (HL24074).

1055. HARVARD MEDICAL SCHOOL, Laboratory of Psychobiology, 25 Shattuck Street, Building B-1, Boston, Massachusetts 02115. NEW ENGLAND REGIONAL PRIMATE RESEARCH CENTER, Department of Behavioral Biology, 1 Pine Hill Drive, Southborough, Massachusetts 01772.

Project Title:
Analysis of Behavior Controlled by Drug Injections.

Principal Investigators:
Morse, W.H.; Spealman, R.D.; Kelleher, R.T., et al.

Objective:
To study pharmacological and environmental determinants of drug dependence by systematically investigating the control of behavior by scheduled injections of drugs (including self-administration of nicotine, morphine, phencyclidine, and cocaine).

Methods or Approach:
Behavior maintained by self-administration of drugs is compared directly with behavior maintained under identical conditions by other consequences, such as presentation of food or termination of electric shock. Research should provide needed quantitative information about the effects of chronic drug administration and suppressive noxious stimuli in relation to drug dependence.

Results to Date:
Under a fixed-interval schedule of nicotine self-administration in squirrel monkeys, responding was well maintained by injections of 30 to 300 μg/kg nicotine. Nicotine-maintained responding could be reduced by presession treatment with the nicotine antagonist mecamylamine or by substitution of saline for nicotine. In a second experiment, responding was maintained under a two-component fixed-ratio schedule of food presentation in which responses during one component (punishment) also resulted in injections of 10 to 30 μg/kg nicotine. Nicotine markedly suppressed responding during the punishment component but not during the alternating nonpunishment components. The suppressant effects of nicotine could be reversed by presession treatment with either mecamylamine or the antianxiety drug chlordiazepoxide or by substitution of saline for nicotine. Nicotine had pronounced effects both as a reinforcer and as a punisher; the nature of the effects depended on the schedule under which nicotine was administered.

Project Dates:
June 1973–November 1990.

Financial Support:
ADAMHA (DA 00499).

References:
(1) Spealman, R.D.; Goldberg, S.R.; Gardner, M.L. "Behavioral Effects of Nicotine: Schedule-Controlled Responding by Squirrel Monkeys." *Journal of Pharmacology and Experimental Therapeutics* 216(3):484-491, 1980. (2) Spealman, R.D.; Goldberg, S.R. "Maintainence of Schedule-Controlled Behavior by Intravenous Injections of Nicotine in Squirrel Monkeys." *Journal of Pharmacology and Experimental Therapeutics* 223(2):402-408, 1982. (3) Goldberg, S.R.; Spealman, R.D. "Maintenance and Suppression of Behavior by Intravenous Nicotine Injections in Squirrel Monkeys." *Federation Proceedings* 41:216-220, 1982.

1056. HARVARD MEDICAL SCHOOL, ALCOHOL AND DRUG ABUSE RESEARCH CENTER, McLean Hospital, 115 Mill Street, Belmont, Massachusetts 02178.

Project Title:
Buprenorphine Effects on Cigarette Smoking.

Principal Investigators:
Mello, N.K.; Lukas, S.E.; Mendelson, J.H.

Objective:
To evaluate the effects of the opioid mixed agonist-antagonist buprenorphine on cigarette smoking.

Methods or Approach:
Daily cigarette smoking was compared in adult men with a history of heroin abuse during a 5-day drug-free baseline, a 14-day period during which subjects were given ascending doses of buprenorphine (0.5 to 8.0 mg/day, s.c.), a 10-day period during which subjects were maintained on 8.0 mg/day buprenorphine or its placebo and could work for i.v. heroin at a simple operant task. After buprenorphine or placebo maintenance and heroin availability, subjects were gradually withdrawn from buprenorphine or detoxified with methadone over 5 days.

Results to Date:
Cigarette smoking increased compared with baseline in seven heroin addicts maintained on buprenorphine for 24 days ($p<0.01$ to 0.001). Significant increases in cigarette smoking were associated with buprenorphine doses of ≥ 2.0 mg/day, and smoking during 10 days of buprenorphine maintenance at 8.0 mg/day was significantly higher than during the buprenorphine induction phase ($p<0.01$). Six subjects given placebo buprenorphine over 14 days showed no change in cigarette smoking. Cigarette smoking increased significantly ($p<0.001$) in the placebo group that self-administered heroin for 10 days. Cigarette smoking (defined by inter-cigarette intervals) was highest during high-dose buprenorphine maintenance or placebo plus heroin administration. Data confirm previous findings that opioid agonist administration is associated with increased smoking and suggest that buprenorphine has primarily agonistic effects on smoking.

Project Dates:
1979–1985.

Financial Support:
NIDA (DA 01676; DA 02519; DA 00101; DA 00064).

1057. HARVARD MEDICAL SCHOOL, NEW ENGLAND REGIONAL PRIMATE RESEARCH CENTER, One Pine Hill Drive, Southborough, Massachusetts 01772.

Project Title:
Behavioral Actions of Nicotine and Abused Substances.

Principal Investigator:
Spealman, R.D.

Objective:

To study pharmacological and environmental factors involved in control of behavior by nicotine in nonhuman primates.

Methods or Approach:

Squirrel monkeys with chronic venous catheters respond by pressing a lever under various schedules of reinforcement involving i.v. injections of nicotine. Under different conditions, responding is (1) maintained by response-produced injections, (2) suppressed by response-produced injections, or (3) maintained by postponement of scheduled injections. Effectiveness of nicotine in controlling behavior is evaluated by (1) systematically varying dose/injection; (2) directly comparing effects of nicotine with effects of other drugs known to control behavior; and (3) determining effects of pretreatment with drugs know to alter actions of nicotine.

Results to Date:

Responding by monkeys was developed and maintained under fixed-interval and second-order schedules of i.v. self-administration. Performancess maintained by self-administration were influenced by dose per injection and by environmental stimuli associated with injections. Responding maintained by scheduled presentations of food was suppressed by superimposing a schedule of response-produced nicotine injection. Level of suppression depended on dose per injection. Suppressive effects of nicotine were attenuated by pretreatment with chlordiazepoxide (antianxiety drug). Responding was also developed and maintained under a schedule of nicotine postponement, and as in other experiments, rates and temporal patterns of responding depended on dose per injection. In all experiments, nicotine effects were blocked by the centrally acting nicotinic antagonist mecamylamine, but not by the peripherally acting antagonist hexamethonium, suggesting that behavioral effects of nicotine are centrally mediated. Results indicate that nicotine can control behavior in disparate, even opposite, ways, depending on conditions of administration.

Future Plans:

Studies will determine conditions under which nicotine can control behavior in disparate ways in the same individual.

Project Dates:

September 1980–August 1985.

Financial Support:

NIDA (DA 02658).

References:

(1) Spealman, R.D.; Goldberg, S.R. "Maintenance of Schedule-Controlled Behavior by Intravenous Injections of Nicotine in Squirrel Monkeys." *Journal of Pharmacology and Experimental Therapeutics* 223:402-408, 1983. (2) Goldberg, S.R.; Spealman, R.D. "Suppression of Behavior by Intravenous Injections of Nicotine or by Electric Shocks in Squirrel Monkeys: Effects of Chlordiazepoxide and Mecamylamine." *Journal of Pharmacology and Experimental Therapeutics* 224:334-340, 1983. (3) Spealman, R.D. "Maintenance of Behavior by Postponement of Scheduled Injections of Nicotine in Squirrel Monkeys." *Journal of Pharmacology and Experimental Therapeutics* 227:154-159, 1983. (4) Goldberg, S.R.; Spealman, R.D.; Risner, M.E., et al. "Control of Behavior by Intravenous Nicotine Injections in Laboratory Animals." *Pharmacology, Biochemistry and Behavior* 19:1011-1020, 1983. (5) Spealman, R.D. "Environmental Factors Determining the Control of Behavior by Drugs. In: Seiden, L.S.; Balster, R.L. (Editors). *Behavioral Pharmacology: The Current Status.* New York, Alan R. Liss, 1985, pp. 149-166.

1058. HARVARD UNIVERSITY, SCHOOL OF DENTAL MEDICINE, 188 Longwood Avenue, Boston, Massachusetts 02115.

Project Title:

Effects of Smokeless Tobacco and Snuff on Oral Mucosa of Experimental Animals.

Principal Investigators:

Shklar, G.; Niukian, K.; Hassan, M., et al.

Objective:

To study the effect of smokeless tobacco on oral mucous membrane.

Methods or Approach:

Sixty male random-bred Syrian hamsters (60 to 90 days old) weighing 100 to 125 g were divided into three equal groups. Group 1 were controls; 10 were untreated and 10 were manipulated with a plastic instrument to mimic placement of tobacco and snuff. In Groups 2 and 3, tobacco or snuff was placed in the right buccal pouch daily using a hollow plastic cylinder. The left buccal pouches of animals in Groups 2 and 3 were also used as controls; 10 in each group were untreated and 10 were manipulated with a plastic instrument. There was a fairly consistent delivery into the pouches of approximately 0.07 g of substance, particularly of finely powdered snuff. Tissues were studied grossly and histologically after 10 or 20 weeks. Mitotic activity was examined (epithelial whole mounts, thymidine, autoradiography) and Langerhans cells were studied using ATP-ase technique on whole mounts.

Results to Date:

Histologic study revealed no significant pathologic changes at either 10 or 20 weeks; however, studies on epithelial whole mounts revealed a statistically significant decrease in mitotic activity and a statistically significant increase in the number of Langerhans cells in animals subjected to daily use of tobacco or snuff for 20 weeks.

Future Plans:

The effect of smokeless tobacco as a promoter or cocarcinogen will be investigated.

Project Dates:

July 1982–June 1985.

Financial Support:

Smokeless Tobacco Research Council.

1059. HARVARD UNIVERSITY, SCHOOL OF DENTAL MEDICINE, 188 Longwood Avenue, Boston, Massachusetts 02115.

Project Title:

Retardation of Experimental Oral Cancer by Topical Vitamin E.

Principal Investigators:

Odukoya, O.; Hawach, F.; Shklar, G.

Objective:

To determine whether vitamin E, when applied locally or topically to hamster buccal pouch mucosa, could exert a similar effect on carcinogenesis as systemic administration of vitamin E.

Methods or Approach:

Golden hamsters were divided into four groups (six males and six females per group) and treated with (1) dimethylbenzanthracene (DMBA), (2) dimethylbenzanthracene (DMBA) and vitamin E, (3) vitamin E only, and (4) no treatment (controls). DMBA was painted on the left buccal pouches three times/week for 7 weeks. Vitamin E was painted on the left buccal pouch three times/week for 4 weeks following DMBA application. Six animals in each group were chosen at random for sacrifice following treatment and the other six were sacrificed 1 week later. Buccal pouches were photographed and tumors were counted and measured. Buccal pouches were excised, fixed in 10 percent formalin, sectioned in paraffin, and stained with hematoxylin and eosin for microscopic study. Determination of statistical results was based on gross number of tumors observed and the student's t-test for paired data was used to determine level of statistical significance.

Results to Date:
All animals in groups 1 and 2 presented some evidence of tumor formation after 11 or 12 weeks. At each sacrifice time, the left buccal pouches of group 2 animals had fewer tumors than those in group 1 and tumors were smaller in diameter. Left buccal pouches of group 2 animals demonstrated not only smaller epidermoid carcinomas but also fewer areas of dysplasia and hyperkeratosis compared with pouches from group 1 animals.

Future Plans:
Studies will include topical application of anticarcinogenic agents other than vitamin E and futher examination of vitamin E inhibition of carcinogenesis.

Project Dates:
July 1982–June 1985.

Financial Support:
Smokeless Tobacco Research Council.

1060. HARVARD UNIVERSITY, SCHOOL OF PUBLIC HEALTH, Department of Epidemiology, 677 Huntington Avenue, Boston, Massachusetts 02115.

Project Title:
A Case-Control Study of Renal Adenocarcinoma.

Principal Investigators:
MacMahon, B.; Maclure, K.M.

Objective:
To (1) improve estimates of the relative risk of renal adenocarcinoma due to tobacco use; (2) test the hypotheses that dietary cholesterol is an important risk factor and that dietary vitamin A is protective; (3) reexamine the hypothesis that coffee and dietary cadmium are risk factors; (4) obtain a clearer understanding of the relationship to ethnic background; (5) explore a number of other hypotheses including etiologic roles for occupational exposures, determinants of hormonal status, and usage of certain drugs; (6) evaluate interactions that are expected to occur between some of the factors; (7) identify modifiable risk factors; and (8) contribute new information relevant to the cancer etiology.

Methods or Approach:
Cases of renal adenocarcinoma are identified by reviewing pathology logs, tumor registries, and medical records at 37 participating hospitals in the greater Boston area. Following physician approval, patients are contacted by mail and by phone to request participation in an hour-long interview at home or at work. Controls, matched for age, sex, and area of residence, are randomly selected from a list of residents in the appropriate town or city. Interviews cover topics listed as risk factors or potential preventive factors. To evaluate selection bias, a shorter version of the questionnaire is mailed to controls who do not agree to be interviewed in person. Risk ratios are being estimated by multivariate conditional logistic regression, controlling for both confounders and potential selection biases.

Results to Date:
A weak positive association with cigarette smoking has been found, but only after controlling for selection biases. Biases prevented findings from contributing to improved estimation of relative risks due to smoking. Findings appear to confirm previously observed associations with obesity, northeastern European ancestry, renal calculi, and use of phenacetin-containing analgesics.

Future Plans:
Final analyses will be made and results published in 1986.

Project Dates:
July 1981–June 1985.

Financial Support:
Harvard School of Public Health; NCI (CA 29723).

1061. HARVARD UNIVERSITY, SCHOOL OF PUBLIC HEALTH, 665 Huntington Avenue, Building 1, Room 1402, Boston, Massachusetts 02115.

Project Title:
Respiratory Effects of Sulfur Dioxide Among Workers in Corn Refining Plants.

Principal Investigators:
Greaves, I.A.; Ferris, B.G., Jr.; Burgess, W.A.

Objective:
To examine respiratory symptoms, lung function, and chest radiographs in a sample of corn refiners exposed to various levels of sulfur dioxide; define exposure–response relationships for sulfur dioxide among workers.

Methods or Approach:
A standard questionnaire, spirometry, and PA chest radiographs were used to study 457 workers. Current exposures to sulfur dioxide, respirable particulates, and water-soluble sulfates were measured by standard sampling and analysis methods.

Results to Date:
Symptoms of mucosal irritation (cough, phlegm production) and intermittent airway narrowing (frequent wheezing, exertional breathlessness) were related to increasing sulfur dioxide levels. Symptom rates were adjusted for possible age and smoking effects by internal standardization. Lung function showed a small detrimental effect of cumulative smoking, but no effects of current or cumulative sulfur dioxide exposure were noted. No specific chest radiograph abnormalities were found in exposed vs. nonexposed workers, and no smoking effects were observed.

Project Dates:
July 1983–May 1985.

Financial Support:
NIOSH.

1062. HARVARD UNIVERSITY, SCHOOL OF PUBLIC HEALTH, 55 Shattuck Street, Boston, Massachusetts 02115.

Project Title:
Randomized Study of Tobacco and Marijuana Smoking Prevention.

Principal Investigators:
McAlister, A. L.; Maccoby, N.; Perry, C.

Objective:
To test the hypothesis that smoking cigarettes or other substances can be prevented through noncoercive persuasive influence.

Methods or Approach:
A 2-year, randomized study of 10 schools was conducted to test the effects of a peer-led preventive program on tobacco and marijuana use among young adolescents. In five sites, two cohorts of sixth or seventh graders were identified. One of each of these matched pairs of cohorts was randomly assigned to receive the program designed to prevent smoking and marijua-

na use. Both cohorts were surveyed at baseline and over 2 years of followup to assess outcomes and analyze processes in health behavior development.

Results to Date:

For tobacco smoking, differences in followup rates between treatment and control groups in inner-city schools were statistically significant ($p < 0.07$); for marijuana smoking, differences were not significant. Smoking rates and rates of change were more variable than expected, suggesting that results from small-scale studies are not easily generalized and that complex experimental programs are not easily disseminated. Overall, it is concluded that some positive results may be obtained from preventive programs of this type, but only with great efforts in implementation. If successfully organized, such interventions may significantly reduce the rate at which young adolescents begin to smoke tobacco and marijuana. Data from the inner-city schools show that a program may be effective even in unfavorable settings, but more research is needed before conclusions can be drawn about the usefulness of social-psychological strategies for substance abuse prevention.

Project Dates:

April 1979–August 1981.

Financial Support:

NICHD (R01-12813-01).

1063. HARVARD UNIVERSITY, SCHOOL OF PUBLIC HEALTH, 665 Huntington Avenue, Boston, Massachusetts 02115.

Project Title:

Effects of Sulfur Dioxide and Respirable Particulates on Health.

Principal Investigators:

Ferris, B.G., Jr.; Speizer, F.E.

Objective:

To determine whether current ambient air quality standards for sulfur dioxide and particulate matter are adequate and to obtain data on exposures to fine particulate matter and acidic aerosols.

Methods or Approach:

Random samples of adults and children have been studied and are being followed at regular intervals. Health effects are monitored with standard questionnaires on respiratory symptoms and home characteristics and with simple tests of pulmonary function. Air monitoring is done at a central site and at various sites in the city. It is anticipated that 150 to 200 hours/city will be monitored for indoor pollution concentrations. Acidic aerosols are also being monitored.

Results to Date:

Maternal smoking and, to some extent, paternal smoking affect the pulmonary function and respiratory symptoms of children living in homes with parents who smoke. There appears to be a dose–response relationship with the number of cigarettes smoked/day by the mother. There is probably an air pollution effect as indicated by a progressive increase in respiratory symptoms as pollution concentrations increase. There is not, however, any change in pulmonary function. Further analyses may identify more significant effects.

Future Plans:

Further studies will be conducted to (1) analyze collected data; (2) follow children through high school; (3) evaluate a new cohort of children to determine whether respiratory health improved as air pollution concentrations declined.

Project Dates:

July 1974–July 1988.

Financial Support:

NIEHS (ES01108); EPA (CR811650); Electric Power and Research Institute (RP 1001).

1064. HARVARD UNIVERSITY, SCHOOL OF DENTAL MEDICINE, Laboratory of Pharmacology, 188 Longwood Avenue, Boston, Massachusetts 02115.

Project Title:

Effects of Nicotine and Benzo(*a*)pyrene on Normal and Ectopic Hormone Production.

Principal Investigator:

Biswas, D.K.

Objective:

To determine the possible molecular mechanisms involved in the inappropriate expression of a gene under the influence of nicotine, benzo(*a*)pyrene (BaP), and dimethylbenzanthracene (DMBA).

Methods or Approach:

Experiments, based on already established properties of two cultured cell systems, examined (1) the effect of nicotine, BaP, and DMBA on hormone production by rat pituitary tumor cells (GH cells) and by human lung tumor cells in culture (ChaGo cells); (2) the possible role of altered base composition of cellular DNA and the role of binding of the chemicals to DNA on the effect of the compounds on hormone production by GH cells and ChaGo cells; and (3) specific RNA synthesis in a cell-free RNA synthesizing system with nuclei isolated from control and treated GH cells and ChaGo cells. Studies will initially be limited to quantitation of prolactin and growth hormone-specific RNA sequences synthesized in the cell-free system by molecular RNA/cDNA hybridization assay.

Results to Date:

Treatment of GH cells with nicotine (0.1 to 300 μg/mL) did not affect growth or significantly alter the general pattern of hormone production. BaP at concentrations >5 μg/mL irreversibly inhibited growth. Sublethal concentrations of BaP did not affect cell growth, amino acid transport, or total protein synthesis or degradation, but did inhibit hormone synthesis by the cells. Concentrations of nicotine that did not affect cell growth or hormone syntheses did modulate both processes in the presence of BaP. A concentration-dependent stimulation of microsomal BaP monooxygenase activity was observed in cells treated with nicotine or BaP. The effect on stimulation of BaP monooxygenase activity appears to be additive. Nicotine also enhanced the association of radioactivity with DNA in (^{3}H)BaP-treated cells. It is concluded that nicotine by itself did not demonstrate any cytotoxic effect or influence hormone synthesis in GH cells; however, it stimulated BaP monooxygenase activity and the interaction of (^{3}H)BaP metabolites with cellular DNA, and modulated BaP-induced inhibition of hormone synthesis in GH cells.

Project Dates:

April 1980–May 1981.

Financial Support:

CTR.

1065. HARVARD UNIVERSITY, VETERAN'S ADMINISTRATION OUTPATIENT CLINIC, 17 Court Street, Boston, Massachusetts 02108.

Project Title:

Informal Self-Help Approaches to Smoking Cessation.

Principal Investigators:

Garvey, A.J.; Bosse, R.

Objective:
To examine types of quitting strategies used by smokers who quit on their own.
Methods or Approach:
A structured interview schedule was used with 200 former smokers and 200 recidivists.
Results to Date:
Strategies or methods for quitting used by successful quitters and recidivists were quite similar. Most subjects quit abruptly rather than gradually reducing consumption, and use of oral substitutes such as candy, gum, or snacks was characteristic of approximately 80 percent. Former smokers were more likely to report higher motivation for quitting, were more likely to switch to cigars and pipes, and were less likely to report urges to smoke in the period shortly after cessation.
Project Dates:
July 1980–August 1983.
Financial Support:
NCI (CA 29479).
References:
Heinold, J.W.; Garvey, A.J.; Goldie, C.L., et al. "Retrospective Analysis in Smoking Cessation Research." *Addictive Behaviors* 7:347-353, 1982. (2) Garvey, A.J.; Bosse, R.; Glynn, R.J., et al. "Smoking Cessation in a Prospective Study of Healthy Adult Males: Effects of Age, Time Period, and Amount Smoked." *American Journal of Public Health* 73:446-450, 1983.

1066. HARVARD UNIVERSITY, VETERAN'S ADMINISTRATION OUTPATIENT CLINIC, 17 Court Street, Boston, Massachusetts 02108.

Project Title:
Psychosocial Stressors, Smoking Cessation and CV Risk.

Principal Investigators:
Garvey, A.J.; Heinhold, J.W.; Plude, D.J., et al.
Objective:
To examine the role of psychosocial stress as a factor in maintaining the tobacco habit; determine whether smoking improves performance on complex problem-solving tasks.
Methods or Approach:
The study sample will consist of 150 smokers, 150 ex-smokers, and 150 never smokers. Subjects will be interviewed using structured interview schedules. Daily stress levels and procedures for coping with stress will be assessed and personality characteristics will be obtained. Subjects will also be tested on cognitive problem-solving tasks that will be presented by a microcomputer.
Results to Date:
Project is in the data collection stage.
Project Dates:
July 1983–July 1986.
Financial Support:
NHLBI (HL 29794).

1067. HARVARD UNIVERSITY, SCHOOL OF PUBLIC HEALTH, 677 Huntington Avenue, Boston, Massachusetts 02115.

Project Title:
Long Term Consequences of Postmastectomy Irradiation.

Principal Investigators:
Hutchison, G.B.; Blitzer, P.H.
Objective:
To determine incidence of fatal coronary artery disease and second primary malignancies following treatment for breast cancer; determine variation in incidences by modality of treatment (radical mastectomy with or without radiotherapy).
Methods or Approach:
A cohort epidemiologic study will be conducted of patients with breast cancer who have been treated by radical mastectomy with or without radiotherapy. Patients will be followed for 11 to 22 years (or to death before this interval) to ascertain incidence of second primary malignancy and mortality from coronary artery disease. Radiation dose to heart and selected malignancy sites will be determined. Analysis will control confounding by major risk indicators. The effect of smoking on coronary heart disease mortality and secondary malignancies will be analyzed.
Results to Date:
Project is in a preliminary phase.
Project Dates:
July 1983–May 1986.
Financial Support:
NCI (5R01CA35479-02).

1068. HARVARD UNIVERSITY, JOHN F. KENNEDY SCHOOL OF GOVERNMENT, Institute for the Study of Smoking Behavior and Policy, 79 Kennedy Street, Cambridge, Massachusetts 02138.

Project Title:
Cabot Conference Series on Smoking Behavior and Policy.

Principal Investigator:
Schelling, T.C.
Objective:
To convene a series of regular conferences for the purpose of exploring key issues in smoking behavior research and policy development.
Methods or Approach:
Each conference will bring together a variety of experts and interested parties in a working environment designed to examine the state of knowledge on a particular issue and to identify opportunities for research and development of new or more effective policies. Each conference will be summarized in a report published by the institute and distributed to a wide audience including government officials at all levels, insurance companies, and others beyond the immediate smoking research community. Conferences will be held four times a year, beginning in March 1985. Possible conference topics include tax policy, advertising, insurance, young smokers and quitters, smoking in the workplace, women smokers, international smoking comparisons, genetics and biochemistry of smoking addiction, the young adult smoker, and smoking by pregnant women.
Results to Date:
Project is in a preliminary phase.
Project Dates:
March 1985–1988.
Financial Support:
Cabot Family Charitable Trust.

1069. HARVARD UNIVERSITY, JOHN F. KENNEDY SCHOOL OF GOVERNMENT, 79 Kennedy Street, Cambridge, Massachusetts 02138.

Project Title:
Institute for the Study of Smoking Behavior and Policy.

Principal Investigator:
Schelling, T.C.
Objective:
To develop new knowledge about smoking behavior; translate

knowledge into programs and policies, both public and private, to reduce prevalence of cigarette smoking.

Methods or Approach:

Beyond establishing a few research projects, the institute hopes to function as a resource center and clearinghouse for researchers and others interested in smoking behavior. It hopes to stimulate awareness and interest in smoking behavior and to encourage researchers to undertake projects investigating related topics, providing researchers with moral support and technical advice. The institute will collect and analyze information on research in smoking behavior, both completed and ongoing, to identify gaps in knowledge about smoking behavior. It will also collect information about researchers nationwide, and alert appropriate individuals to research opportunities identified. The institute will also offer researchers assistance and advice on research design and grant-seeking and, by creating a network of researchers with similar interests, will facilitate improved communication and cooperation and prevent duplications of effort that stem from researchers' perceived isolation from others in their field. To stimulate interest of the private sector and public officials, the institute will maintain contacts with the press and other news media and will provide a research information service featuring a specialized collection of reference and research literature and extensive user support to make the information accessible to the layperson. The institute will also conduct research projects on the following topics identified by a panel of experts: natural history of smoking behavior, demography and social epidemiology of smoking, intervention research, tobacco dependence, policy analysis, and social history of smoking.

Results to Date:

Needs analysis has been initiated to determine how the institute can be of service to the research community. Funding has been secured for a 3-year program of policy conferences.

Future Plans:

The institute will convene a series of conferences on smoking behavior and policy; publish discussion papers on a variety of topics; and create a computerized database for more effective use of information on research and researchers' interests.

Project Dates:

May 1984–continuing.

Financial Support:

Carnegie Corporation; W.K. Kellogg Foundation; Conrad N. Hilton Foundation.

1070. HARVARD UNIVERSITY, JOHN F. KENNEDY SCHOOL OF GOVERNMENT, Institute for the Study of Smoking Behavior and Policy, 79 Kennedy Street, Cambridge, Massachusetts 02138.

Project Title:

Analysis of the Demography of Smoking.

Principal Investigator:

Stoto, M.A.

Objective:

To (1) gather data on smoking behavior; (2) assess quality of data; (3) identify gaps and deficiences in available data; (4) develop better methodologies for analysis; and (5) evaluate potential benefits of targeting particular groups for interventions by gathering and assessing information on the health consequences of quitting.

Methods or Approach:

As part of a broader effort to design and evaluate public policies for smoking cessation or prevention, this project will review and assess the demography of smoking (i.e., age, race, sex, and other health and socioeconomic characteristics of current smokers and those who start, stop, and start again). Aggregate and individual data from censuses, national surveys, and other more restricted populations will be searched and evaluated, especially comparative data from as many countries as possible, to learn which behavior patterns are unique and which are universal. Special attention will be given to (1) differences in groups as defined by sex, race, age, education, occupational characteristics, family status, and geographical location; (2) chronological patterns (within individuals) of onset, cessation, relapses, repeated cessation attempts, and ultimate success or failure; (3) associates on smoking and nonsmoking, quitting, and relapse; and (4) similarities with other compulsive behaviors.

Results to Date:

Project is in a preliminary phase.

Project Dates:

February 1985–September 1985.

Financial Support:

NCI (N01CN35011).

1071. LAHEY CLINIC MEDICAL CENTER, 41 Mall Road, Burlington, Massachusetts 01803.

Project Title:

Lung Cancer in Women.

Principal Investigator:

Andrews, J.L., Jr.

Objective:

To investigate the etiological factors in diagnosed cases of lung cancer, including cigarette smoking, sex, and environmental exposures.

Methods or Approach:

All lung cancer cases seen at the Lahey Clinic, a large multispecialty clinic in Boston, were analyzed. Subjects were identified through previous studies done between 1956 and 1972 (approximately 2,000 cases) and updated to 1980 to cover a 24-year period. Additional data, including sex and age, were obtained from the Clinic Tumor Registry. Since there is an increased proportion of women among the cases, further analysis was done on the female cases, including histological confirmation of tumor cell type and Kreyberg classification.

Results to Date:

Results show that the greatest increase in lung cancer in women is among smokers who have Kreyberg Group I (smoking-related) tumors. Preliminary results have been published.

Project Dates:

1974–continuing.

Financial Support:

Lahey Clinic Medical Center.

References:

(1) Beamis, J.; Andrews, J.; Stein, A. "Changing Epidemiology of Lung Cancer: Increasing Incidence in Women." *Medical Clinics of North America* 59:315-325, 1975. (2) Andrews, J.L., et al. "Lung Cancer Occurs More Frequently in Smoking Women: A Review of 1752 Cases 1957-1980." (Abstract) *American Review of Respiratory Disease* 123:651, 1981.

1072. LAHEY CLINIC MEDICAL CENTER, 41 Mall Road, Burlington, Massachusetts 01803.

Project Title:

Smoking Reduction in a Private Hospital and Ambulatory Clinic.

Principal Investigator:

Andrews, J.L., Jr.

Objective:
To form a comprehensive effective policy for smoking reduction among patients, visitors, and staff in a private hospital/ambulatory care facility (Lahey Clinic Medical Center).

Methods or Approach:
The effective aspects of the program will be assessed and, when necessary, the smoking reduction policy will be altered to be more effective. A smoking policy task force will be formed with hospital-wide representation including physicians, nurses, administrators, and medical staff and monthly meetings will be held. Questionnaires will be administered to staff and patients about smoking habits and attitudes regarding policies limiting smoking before and after implementation of a comprehensive hospital smoking reduction policy.

Results to Date:
Results of reduction policy formulation and implementation over a 5-year period at the New England Deaconess Hospital (Boston) have been published, and lessons learned are being applied at the Lahey Clinic. Hospitals must take a leadership role in forming effective programs to reduce smoking and can serve as models in reducing smoking in other workplace situations. Program assessment must be very honest about what works and what does not work.

Project Dates:
September 1984–September 1989.

Financial Support:
Lahey Clinic Medical Center.

Reference:
Andrews, J. "Reducing Smoking in the Hospital: An Effective Program." *Chest* 84:206-209, 1983.

1073. MASSACHUSETTS GENERAL HOSPITAL, Departments of Dermatology and Hematology-Oncology, Boston, Massachusetts 02114.

Project Title:
Cigarette Smoking and Malignant Melanoma. Prognostic Implications.

Principal Investigators:
Koh, H.K.; Sober, A.J.; Day, C.L., Jr., et al.

Objective:
To determine whether or not the extra risk for melanoma in smokers becomes negligible after accounting for tobacco-induced immune dysfunction that facilitates the spread of metastases.

Methods or Approach:
Heavy cigarette smoking (current smoking with >15 pack-years of smoking) and 13 other variables were tested for ability to predict death in 196 patients with clinical Stage I melanoma. A stepwise proportional hazards general linear model (Cox multivariate analysis) was used.

Results to Date:
Data indicate that although cigarette smoking as a single variable is an adverse prognostic marker ($p=0.0065$), it has only suggestive prognostic significance once thickness factors are taken into account ($p=0.0747$). People who stopped smoking had the same survival as nonsmokers. Clinical Stage I patients with melanoma who were heavy smokers presented with thicker lesions than nonsmoking counterparts ($p=0.037$). Cigarette smoking may play a role in the biologic behavior of melanoma by mediating an effect on thickness, but it need not be considered as an independent stratification criterion when analyzing results of melanoma prognosis or treatment.

Financial Support:
Marion Gardner Jackson Trust.

Reference:
Koh, H.K.; Sober, A.J.; Day, C.L., Jr., et al. "Cigarette Smoking and Malignant Melanoma." *Cancer* 53(11):2570-2573, June 1, 1984.

1074. MASSACHUSETTS GENERAL HOSPITAL, Medical Practices Evaluation Unit, Boston, Massachusetts 02114.

Project Title:
Smoking Cessation by Patients Recovering From Coronary Artery Bypass Surgery.

Principal Investigators:
Rigotti, N.; Cleary, P.; Leaf, A., et al.

Objective:
To determine rate at which smokers resume smoking after the period of enforced nonsmoking required during and after coronary artery bypass surgery; determine whether a brief, in-hospital intervention program would increase long-term abstinence from smoking.

Methods or Approach:
A randomized controlled trial will be conducted. Patients in the intervention group will receive a self-help smoking cessation booklet, will watch a videotape, and will be visited by a nurse-educator during stay in post-surgery unit. Intervention and control groups will be followed closely after discharge, for a period of 1 year.

Results to Date:
Project is in a preliminary phase.

Future Plans:
If the pilot program is successful, it will be extended to a larger trial.

Project Dates:
February 1985–January 1987.

Financial Support:
AHA.

1075. MASSACHUSETTS GENERAL HOSPITAL, Hypnosis and Psychosomatic Medicine, 32 Fruit Street, Boston, Massachusetts 02114.

Project Title:
Microcomputer-Assisted Relaxation.

Principal Investigators:
Baer, L.; Surman, O.S.

Objective:
To design a computer software program for anxiety/stress reduction and habit control; extend program for use in smoking cessation.

Methods or Approach:
An interactive computer program was developed for the Apple IIc computer. Using high resolution graphics, the program is composed of sections for muscle relaxation, controlled breathing and eye fixation, and guided imagery. The components are common to most clinical approaches to stress reduction and hypnosis. Additional programs for habit control will be added to the "core" module.

Results to Date:
Phase I testing of the relaxation program "Intermission" (copyright 1984) has been completed with 20 healthy hospital volunteers. A significant reduction in both state and trait measures was demonstrated for each of two supervised exposures to the program.

Future Plans:
Phase II testing of the relaxation program, which will begin in 1985, will compare the relaxation program with a placebo

computer program. Design and testing of an interactive smoking cessation program will also begin in 1985.

Project Dates:
May 1984–continuing.

1076. MASSACHUSETTS INSTITUTE OF TECHNOLOGY, Francis Bitter National Magnet Laboratory, 170 Albany Street, Cambridge, Massachusetts 02139.

Project Title:
Clearance of Magnetic Dust from Lungs of Smokers.

Principal Investigators:
Cohen, D.; Brain, J.D.; Smith, T.J., et al.

Objective:
To measure the difference in long-term clearance rate of dust from the lungs of smokers vs. nonsmokers.

Methods or Approach:
A ferromagnetic dust is used as a tracer in an inhalation study of smokers vs. nonsmokers. The amount of dust retention is measured by a sensitive magnetometer approximately every 3 weeks.

Results to Date:
The time for the long-term clearance of dust from human lungs was measured in three heavy cigarette smokers and nine nonsmokers who inhaled a harmless trace amount of magnetic dust Fe_3O_4. A clearance curve was determined for each subject. The magnetic tracer method allows clearance to be safely followed for a much longer time than with radioactive tracer methods. The dust clearance in the smokers was considerably slower than that in the nonsmokers. After a year, 50 percent of the original dust deposit remained in the lungs of the smokers whereas only 10 percent remained in the lungs of the nonsmokers. This impaired clearance of Fe_3O_4 suggests impaired clearance in smokers of other dusts, e.g., toxic occupational and urban dusts. Higher retention of these dusts may contribute to the higher incidence of lung diseases in smokers.

Future Plans:
In a three-part study, a magnetic dust tracer will be inhaled in six heavy smokers (high tar and nicotine cigarettes), three heavy smokers who quit, three heavy smokers (low tar and nicotine cigarettes), and three nonsmokers to determine if (1) retention is a function of nicotine and tar content, and (2) dust retention in nonsmokers is similar to that in ex-smokers. The second part of the study will measure magnetic dust tracer content in the lungs of 10 heavy smokers and 10 nonsmokers with long urban dust exposure histories and in 10 smoking and 10 nonsmoking arc welders. In the third part, the dust content from sections of autopsied lung will be measured magnetically and chemically. At least 150 subjects including smokers, nonsmokers, and urban dwellers will be studied in order to (1) correlate the amounts of magnetic dust and total dust in the lung with lung pathology, and (2) determine if magnetic measurements are an appropriate index for total dust retention and lung pathology.

Project Dates:
July 1979–1983.

Financial Support:
NHLBI (HL24540).

Reference:
Cohen, D.; Arai, S.F.; Brain, J.D. "Smoking Impairs Long-Term Dust Clearance From the Lung." *Science* 204(4392):514-517, May 4, 1979.

1077. MASSACHUSETTS INSTITUTE OF TECHNOLOGY, Department of Applied Biological Sciences, Cambridge, Massachusetts 02139.

Project Title:
Dosimetry of 4-Aminobiphenyl in Humans Using Blood Protein Adducts.

Principal Investigators:
Tannenbaum, S.R.; Skipper, P.L.; Bryant, M.S.

Objective:
To develop methods for quantitation of human exposure to carcinogens found in cigarette smoke, such as 4-aminobiphenyl (ABP).

Methods or Approach:
An estimate of tissue dose in exposed individuals is determined by isolation of blood proteins (hemoglobin and albumin) and level of carcinogen-protein adducts by various analytical procedures. Using dose–response relationship and other parameters on kinetics of formation and accumulation of adducts in the rat model, adduct levels can then be used to estimate daily human exposure values.

Results to Date:
A sufficiently sensitive method has been developed for analysis of ABP-hemoglobin adducts. Preliminary studies with human samples have shown detectable levels of ABP in blood of smokers and nonsmokers. Extrapolation from the rat model to the human yielded estimated intake values of up to 40 ng ABP/day.

Future Plans:
Analytical procedures for quantitation of 4-ABP-albumin adducts will be developed and used in conjunction with the hemoglobin adduct methodology. Additional blood samples will be analyzed from humans with known smoking histories and certain dietary characteristics.

Project Dates:
October 1982–continuing.

Financial Support:
NIEHS (5P01ES000597-13).

1078. PETER BENT BRIGHAM HOSPITAL, CHANNING LABORATORY, 180 Longwood Avenue, Boston, Massachusetts 02115.

Project Title:
A Prospective Cohort for Risks in Breast Cancer.

Principal Investigator:
Speizer, F.E.

Objective:
To follow prospectively a cohort of approximately 121,000 women in whom exposure to oral contraceptives, estrogens, cigarettes, and hair dyes has been documented.

Methods or Approach:
Morbidity and mortality for a variety of cancers (including breast, endometrial, ovarian, and lung) and cardiovascular events will be followed. The approach is by mailed questionnaire, with further documentation of events by review of hospital records and pathologic specimens. The cohort was defined from the register of Registered Nurses, collected by the American Nurses' Association in 1972. The women, who were 30 to 55 years of age in 1972 and recorded as being married, responded to an inquiry in 1976 that also collected information on menstrual history, height, weight, current contraceptive status, and family history of myocardial infarction and breast cancer in female relatives. Parental occupations were used to estimate social status at age 16. Personal past medical events related to cardiovascular and thromboembolic disease and

benign and malignant breast and other cancers were also collected. In 1980, a detailed dietary assessment was added. Variables will be used in multivariate models to define levels of risk in 1982.

Results to Date:
Results are not yet available.

Financial Support:
NCI (3R01CA23645-05).

1079. POLICY ANALYSIS INC., 1577 Beacon Street, Brookline, Massachusetts 02146.

Project Title:
The Economic Costs of Smoking and Benefits of Smoking Cessation for Individual Smokers.

Principal Investigators:
Oster, G.; Colditz, G.A.; Kelly, N.L.

Objective:
To estimate the expected lifetime economic consequences of cigarette smoking for individual smokers; estimate the expected economic consequences of smoking cessation for individual smokers.

Methods or Approach:
Estimates of the economic costs of cigarette smoking were obtained by combining age- and sex-specific estimates of lifetime economic costs of three smoking-related diseases (lung cancer, coronary heart disease, and emphysema) with estimates of smokers' increased likelihood of developing these illnesses in each remaining year of life relative to nonsmokers. Estimates of economic consequences of quitting were based on disease cost estimates and on estimates of ex-smokers, probability of future disease relative to continuing smokers. Estimates of economic costs and benefits of quitting were calculated separately for men and women between 35 and 79 years of age who were light, moderate, or heavy smokers.

Results to Date:
Projected costs of cigarette smoking, which varied considerably by sex, age, and amount smoked, were significant for all groups of smokers; e.g., for a 40-year-old man, costs ranged from 20,000 dollars (less than one pack/day) to more than 56,000 dollars (more than two packs/day). Similarly, economic benefits of cessation were significant for all groups; for the 40-year-old man, benefits of quitting ranged from 11,000 dollars (less than a pack/day) to almost 34,000 dollars (more than two packs/day).

Project Dates:
September 1982–May 1984.

Financial Support:
Merrell Dow Pharmaceuticals Inc.

1080. TUFTS-NEW ENGLAND MEDICAL CENTER, DIVISION OF CLINICAL PHARMACOLOGY, 171 Harrison Avenue, Boston, Massachusetts 02111.

Project Title:
Effect of Cigarette Smoking on Drug Disposition.

Principal Investigators:
Greenblatt, D.J.; Shader, R.I.; Ochs, H.R.

Objective:
To evaluate alterations in drug disposition and drug sensitivity associated with cigarette smoking.

Methods or Approach:
The pharmacokinetic and pharmocodynamic effects of single doses of a number of drugs are being performed on heavy cigarette smokers and in nonsmoking controls.

Results to Date:
Smoking may or may not accelerate clearance of drugs, depending on the pathway of the drug in question and the age and sex of the patient.

Project Dates:
June 1972–continuing.

Financial Support:
NIH; NIMH (MH-34223).

1081. U.S. ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE, U.S. ARMY NATICK LABORATORIES, Natick, Massachusetts 01760

Project Title:
The Effect of Environmental Conditions and Sustained Operations on Performance of Soldiers Wearing NBC Protective Gear.

Principal Investigators:
Fine, B.J.; Kobrick, J.L.; Johnson, R.

Objective:
To determine effects of heat, cold, humidity, and sustained operations on performance of perceptual and cognitive tasks while wearing NBC protective clothing.

Methods or Approach:
Laboratory (climatic chambers) studies are conducted under various hot-wet, hot-dry, and cold conditions with appropriate controls. Soldiers perform cognitive, perceptual, and motor tasks for 7 hours while wearing NBC protective clothing or suitable control clothing. Tasks center on operations of an artillery fire direction control center. Two weeks of intensive training precedes experiment. Personality tests, vision tests, and questionnaires (including questions on smoking habits) are employed.

Results to Date:
Data are being analyzed; results are not yet available.

Future Plans:
Depending on study results, other environmentally extreme conditions (with male and female soldiers) will be explored.

Project Dates:
April 1984–continuing.

Financial Support:
DOD.

1082. UNIVERSITY OF LOWELL, Department of Biological Sciences, Lowell, Massachusetts 01854.

Project Title:
Nicotine Induced Changes in Primate Lipoproteins.

Principal Investigators:
Hojnacki, J.L.; Mulligan, J.J.; Cluette-Brown, J.E.

Objective:
To determine whether chronic oral intake of nicotine by nonhuman primates alters plasma lipoprotein composition and metabolism.

Methods or Approach:
Eighteen yearling male atherosclerosis-susceptible squirrel monkeys were divided into (1) control (isocaloric liquid diet twice/day) and (2) nicotine animals (liquid diet supplemented with nicotine at 6 mg/kg body weight/day). Plasma cholesterol, triglyceride, and glucose were measured in fasted monkeys monthly by enzymatic/colorimetric assays. Very low density (VLDL), low density (LDL), and high density (HDL) lipoproteins were isolated at 6, 12, and 24 months by density gradient ultracentrifugation. After 15 months, fasted monkeys from each group were injected with ^{131}I LDL plus ^{125}I HDL apoprotein, plasma samples were collected, and fractional

catabolic (FCR) and absolute catabolic (ACR) rates were calculated from decay curves. After 24 months, fasted monkeys from each group were injected i.v. with ^{1} LDL and ^{14}C HDL cholesteryl ester, plasma was collected at timed intervals, and radioactivity was measured in HDL and VLDL-LDL separated by heparin manganese precipitation. Fecal samples were collected for 24 hours after isotope injection for quantitation of sterol and bile acid mass and radioactivity.

Results to Date:

Nicotine-treated primates had significantly more plasma cholesterol, glucose, and LDL cholesterol and protein but lower amounts of VLDL protein and a reduced HDL cholesterol/plasma cholesterol ratio indicative of an atherogenic lipoprotein profile. Although LDL and HDL FCRs were similar in both groups, ACRs for both LDL and HDL were significantly lower in nicotine animals, suggesting an impairment in lipoprotein production. In addition, nicotine monkeys had delayed removal of radiolabeled LDL cholesteryl ester from the plasma compartment, accelerated transfer of cholesteryl ester from HDL to VLDL-LDL, and reduced fecal sterol output. Thus, nicotine-induced elevations in atherogenic LDL are the result of (1) impaired clearance, and (2) accentuated transfer of lipid from HDL. It is concluded that oral nicotine, independent of other tobacco components, can induce pathophysiological alterations in lipoprotein composition and metabolism.

Future Plans:

The relationship between oral nicotine, circulating sex hormones, and lipoprotein metabolism will be investigated.

Project Dates:

July 1982–December 1985.

Financial Support:

CTR.

1083. UNIVERSITY OF MASSACHUSETTS MEDICAL CENTER, 55 Lake Avenue, North, Worcester, Massachusetts 01605.

Project Title:

Physician Attitudes and Practices in Cigarette Smoking Intervention With Their Patients.

Principal Investigators:

Ockene, J.; Kahn, K.; Raia, T., et al.

Objective:

To examine physicians' attitudes and practices in cigarette smoking intervention and in other disease preventions; determine the relationship of specific physician intervention practices and demographic factors with reported preparation and success in intervening with patients who smoke.

Methods or Approach:

Questionnaires were sent to 600 physicians practicing in a medium-sized city and the surrounding area. In addition to a brief demographic profile, physicians were also asked about their attitudes toward smoking intervention, their intervention practices, other disease prevention attitudes and practices, and their expectation of intervention success and assessment of preparation for helping patients change cigarette smoking behavior.

Results to Date:

A 50 percent response was received, and a second mailing is in progress; results are not yet available.

Future Plans:

Data from the project will be used to help develop intervention practices for use by physicians with patients who smoke.

Project Dates:

January 1984–June 1985.

1084. UNIVERSITY OF MASSACHUSETTS MEDICAL CENTER, 55 Lake Avenue North, Worcester, Massachusetts 01605.

Project Title:

Patients' Reports of Physician Smoking Intervention Practices.

Principal Investigators:

Ockene, J.K.; Raia, T.J.; Goldberg, R., et al.

Objective:

To (1) examine physician smoking intervention practices as reported by patients in different clinical settings; (2) determine prevalence of physician smoking intervention practices among different patient groups; (3) establish whether such practices are influenced by patient's age, sex, or health status and physician expectation of success or preparedness; (4) establish whether patients believe physicians can or do influence smoking behavior; and (5) what interventions patients find most helpful.

Methods or Approach:

Patients were those seen by physicians in a primary care clinic, a cardiology clinic, and a pulmonary clinic. Subjects were asked to complete a questionnaire assessing sociodemographic background, smoking history, perceived physician smoking interventions, and possible physician influence. A chart review was performed on each smoker and ex-smoker to extract information concerning smoking-related diseases and physician notes on patient smoking behavior. Clinic physicians were administered a 50-item questionnaire designed to determine reported smoking intervention and other disease prevention practices and expectations of success and preparedness in changing smoking behavior of patients.

Results to Date:

Preliminary analyses indicate patients seen by pulmonologists and cardiologists were significantly more often men and tended to be older than patients seen by primary care physicians. Of borderline significance is the clinic distribution of smokers, ex-smokers, and nonsmokers; primary care contained higher percentages of current and nonsmokers, while cardiology and pulmonary contained higher percentages of ex-smokers. The mean age of ex-smokers was significantly higher than that of current smokers. Smokers who reported having received physician intervention during a cessation attempt were older, were more often men, and had smoked longer than patients who had not received physician assistance. These findings were statistically significant. The mean number of attempts to stop smoking and the mean length of time smoking were both significantly higher for smokers receiving intervention from their current physician than those who did not receive intervention.

Future Plans:

Integrated results from physician and patient data sets will be used to suggest improved intervention strategies for physicians' use with patients and to develop effective educational programs for training physicians. The primary goal is to help physicians help patients stop smoking.

Project Dates:

August 1983–February 1985.

Financial Support:

University of Massachusetts Medical Center.

1085. UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL, 55 Lake Avenue, North, Worcester, Massachusetts 01605.

Project Title:

Phase Out Smoking Cessation Program.

Principal Investigators:
Ockene, J.; Donnelly, G.

Objective:
To implement and evaluate the effectiveness of a behavioral modification program designed to enable smokers to quit; evaluate the psychosocial and demographic factors that may affect cessation outcome.

Methods or Approach:
The program includes (1) an option for participants to join either a fast track group (immediate quitters) or a slow track group (smokers who prefer to reduce consumption prior to quitting); (2) group support and mutual assistance; (3) subject participation in recordkeeping, stress reduction/relaxation training, goal setting, and other self-control techniques; (4) group meetings held at different intervals during a 6-week period in addition to a general orientation session; (5) followup meetings over a 1-year period; (6) opportunity for smokers to work with personal physicians in choosing whether or not to use nicotine chewing gum as an aid; and (6) determination by the individual smoker as to a quit date. Smoking cessation can start almost immediately or after several weeks of "nicotine fading."

Results to Date:
Of the 65 persons referred by physicians, 48 enrolled in the program after the orientation session; 27 joined the fast track group, and 21 participated in the slow track program. Results show that 66 percent of the fast track group reported cessation at the last session attended compared with only 28 percent of the slow track group; (2) 40 percent of the fast group used nicotine gum compared with only 4 percent of the slow group; (3) 3 percent of those who reported continued smoking in the fast group were using nicotine gum at the last session attended, while none of the slow group was using the gum; and (4) 3 percent reporting cessation in the fast group had carbon monoxide levels >10 ppm at the last session attended compared with 9 percent in the slow group that reported cessation at the last session.

Future Plans:
Participants will be followed for a full year to determine changes in smoking status. Baseline psychosocial, demographic, and smoking history data are being analyzed to determine factors affecting short-term success and factors that may affect the decision whether or not to use nicotine gum. Further analyses will be conducted to determine factors affecting long-term success after 6- and 12-month followup.

Project Dates:
May 1984–July 1985.

Financial Support:
Health Improvement Systems.

1086. UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL, 55 Lake Avenue, North, Worcester, Massachusetts 01605.

Project Title:
Relationship of Pyschosocial and Demographic Factors to Smoking Cessation Following a Myocardial Infarction.

Principal Investigators:
Ockene, J.; Rippe, J.; DeCosimo, D., et al.

Objective:
To investigate possible psychosocial and demographic factors that may determine success in smoking cessation among people who have experienced a myocardial infarction.

Methods or Approach:
Myocardial infarct patients at a university medical center were interviewed 2 days after being moved from an intensive care unit to a hospital room. From questionnaires completed by patients, information was obtained on health locus of control, personal adjustment, smoking environment, attitudes toward smoking, peak number of cigarettes smoked, health habits, and demographic variables of sex, education, and occupation. Before leaving the hospital, all patients were encouraged to quit smoking and were warned about the health hazards associated with smoking, especially for anyone with coronary artery disease. If difficulties in quitting were encountered, a special counselor was consulted to help with behavior change. Followup mailings were sent out 6 months after hospital discharge to determine smoking status.

Results to Date:
To date, 150 cases have been entered, but results have not been analyzed.

Future Plans:
Followup will be also be made after 12 months. A supplementary investigation is planned to examine prognosis and mortality rates among patients with differences in smoking status and complications of myocardial infarct.

Project Dates:
July 1983–July 1985.

Financial Support:
University of Massachusetts Medical School.

1087. UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL, Division of Preventive and Behavioral Medicine, 55 Lake Avenue, North, Worcester, Massachusetts 01605.

Project Title:
The Relationship of Psychosocial Factors and Nursing Specialties to Cigarette Smoking Behavior Among Nurses.

Principal Investigators:
Ockene, J.; Tannenbaum, T.N.; Goldberg, R.L., et al.

Objective:
To (1) determine the prevalence of cigarette smoking among various nursing groups and a comparison group of teachers; (2) identify factors associated with smoking among nurses, with particular examination of the association of psychosocial factors, job stress, stage of lifecycle, and cigarette smoking; and (3) identify interventions and approaches that would be most effective in facilitating cigarette smoking cessation in various target nursing groups.

Methods or Approach:
The study group includes approximately 1,200 staff nurses (home care and acute and chronic hospital care), 225 student nurses, and 200 high school teachers. A questionnaire has been administered to all groups to determine smoking behavior and attitudes, occupational history, occupational and personal stress, health behavior, and personal and demographic variables.

Results to Date:
After three mailings, response has been 79 percent for staff nurses, 64 percent for student nurses, and 75 percent for teachers. Results are being analyzed.

Future Plans:
Results will be used to plan smoking cessation programs for nurses. A further study will be made to compare smoking attitudes and behaviors of student nurses with those of other students.

Project Dates:
July 1983–June 1985.

Financial Support:
Institutional Biomedical Research Support Grant (SO7RR5712).

1088. UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL, 55 Lake Avenue, North, Worcester, Massachusetts 01605.

Project Title:
Relationship of Psychosocial Factors to Smoking Status After the Development of Ischemic Heart Disease (IHD).

Principal Investigators:
Ockene, J.; Williams, J.; Rippe, J., et al.
Objective:
To explore the demographic and psychosocial factors affecting smoking status in patients hospitalized with ischemic heart disease (IHD); use the findings to suggest improved strategies for intervention programs.
Methods or Approach:
Patients hospitalized with IHD were classified into Group 1 (119 who had experienced another cardiac event prior to present hospitalization) and Group 2 (81 who were hospitalized with a first event). On the second day of transfer from the coronary unit to the floor, participants were interviewed and administered questionnaires that assessed their response to the disease, cigarette smoking history, psychosocial and demographic data, medical history, and other coronary risk factor data. Psychosocial variables measured were health locus of control, personal adjustment, smoking environment, attitudes toward smoking, and health habits; demographic data included age, sex, education, and occupation. Patients were subdivided into never smokers, ex-smokers, and current smokers. Univariate analyses were completed for recurrent event patients and multivariate analysis of the difference between groups was performed to determine factors related to smoking status after IHD onset.
Results to Date:
Individuals who had already had a cardiac event are significantly older and have significantly higher scores on chance health locus of control than those who had not. Ex-smoker rates in the two groups indicate that the occurrence of an event and increasing age have a significant effect on whether a smoker will quit. Individuals who continue to smoke following an IHD event are in lower occupational and educational levels, have less negative attitudes toward smoking, smoke a higher number of cigarettes when smoking heaviest, and have a tendency toward being more anxious than ex-smokers. Age is univariately an important discriminator, but its importance in multivariate analysis is as a modifier of the effect of the noted variables. Thus, the effect of education and peak number of cigarettes smoked is increased by age, while the effect of negative smoking attitudes and occupation are decreased for older people.
Project Dates:
July 1983–December 1984.

1089. UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL, Department of Medicine, 55 Lake Avenue, North, Worcester, Massachusetts 01605.

Project Title:
Relapse Factors in Long Term Maintenance of Smoking Cessation.

Principal Investigators:
Camic, P.M.; Donnelly, G.; DeWit, H., et al.
Objective:
To determine those factors that affect relapse in ex-smokers who have participated in a smoking cessation program.
Methods or Approach:
In the investigation of two ongoing clinical treatment programs (University of Massachusetts and University of Chicago), patients are assigned to either group or individual treatment approaches depending on personal preferences, ability to pay, scheduling, and clinical determination. Patients who complete the program are followed for 5 years. Data from phone interviews (every 6 months) and clinic visits (12 and 24 months, to date) have been obtained. During clinic visits, patients receive carbon monoxide monitoring and are questioned in detail about relapse episodes, with particular attention to use of coping strategies. Analytic induction is used in gathering data on relapse episodes, and information about episodes is incorporated into the maintenance phase of the clinical program once a year so that the most clinically useful components are retained and strengthened.
Results to Date:
Of 29 patients followed for 2 years, 56 percent remain abstinent. Among 76 followed for 1 year, there was a 63 percent abstinence rate. Of these 105 patients, 51 percent were male, 89 percent were white; mean age was 41.3 years, mean years of smoking was 21.3. No significant differences were found between relapsers and ex-smokers on these variables, but abstainers tended to be slightly older, had smoked longer, and had made more attempts to quit. Subjects who relapsed did so during a stressful life event (89 percent) or during a time of relaxation or leisure (11 percent). Of the stressful life events, nearly 60 percent were unexpected events (e.g., divorce, job loss, death of loved one, IRS audit, financial problems). Patients reported no repertoire to cope with situations or events. It is interesting to note that 78 percent of relapses occurred during the first 4 months after cessation. Results have led to several program changes; the number of sessions has been increased from 8 to 10, and the program now spans 15 weeks rather than the previous 8 weeks, with the hope that with a longer maintenance program, fewer relapse episodes will occur.
Project Dates:
October 1981–December 1986.
Financial Support:
University of Massachusetts Medical School.

1090. UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL, 55 Lake Avenue, North, Worcester, Massachusetts 01605.

Project Title:
Inflammatory Aspects of Atherosclerosis.

Principal Investigators:
Joris, I.; Majno, G.
Objective:
To determine if smoking induces margination and diapedesis of mononucleated cells into the intima and/or if it acts synergistically in aggravating arteriosclerosis (ATS); establish whether this relationship can be demonstrated quantitatively.
Methods or Approach:
Rats are used to test the effect of smoking alone and in combination with hypercholesterolemia. Carboxyhemoglobin levels will be checked to determine smoke exposure. Rats will be exposed to smoke (using a new, well-controlled smoking machine for rat) for different periods of time (3, 10, and 60 days); 12 hours after the last exposure, animals will be injected with permeability tracers before perfusion-fixation. The aorta will be used for (1) cellular counts related to margination/diapedesis; (2) permeability studies by transmission electron microscopy, and (3) scanning electron microscopic examination of a possible role of platelet adhesion and other surface

changes. The 60-day experimental protocol will be used for rats on the hypercholesterolemic diet.

Results to Date:
The first smoke-exposure machine built by the Tobacco and Health Research Institute will be installed at the beginning of June 1985; therefore, no results related to the effects of smoking are available. Results with hypercholesterolemic rats are very reproducible, and methods for quantitating the number of adherent cells is also well tested.

Project Dates:
June 1985–September 1987.

Financial Support:
NHLBI (HL 33529).

1091. UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL, 55 Lake Avenue, North, Worcester, Massachusetts 01605.

Project Title:
Physician Delivered Smoking Intervention Project.

Principal Investigators:
Ockene, J.; Goldberg, R.J.; Stephenson, W.P.

Objective:
To (1) evaluate relative effectiveness of two levels of physician intervention (minimal and maximal) and two levels of followup (telephone and mail) in helping patients quit smoking; (2) test effectiveness of nicotine gum as an adjunct to maximal physician intervention; and (3) develop teaching tools for physician training in counseling techniques.

Methods or Approach:
In the randomized controlled trial, smokers seen at two clinics will be randomly assigned to one of five treatment conditions: (1) maximal physician intervention, maximal followup, nicotine gum; (2) maximal physician intervention, maximal followup; (3) maximal physician intervention, minimum followup; (4) minimal physician intervention, maximal followup; and (5) minimal physician intervention, minimal followup. Maximal physician intervention will consist of guided questioning counseling techniques, for which resident physicians will be trained prior to patient recruitment.

Results to Date:
Project is currently in the development and pilot testing stage. Tools are being developed for training in counseling techniques and data collection forms and randomization and data management techniques are being developed.

Project Dates:
September 1984–August 1989.

Financial Support:
NCI (1R01CA38360-01).

1092. UNIVERSITY OF MASSACHUSETTS, MEDICAL CENTER, Department of Family Medicine, 55 Lake Avenue, North, Worcester, Massachusetts 01605.

Project Title:
Smoking and Motor Vehicle Accidents.

Principal Investigators:
DiFranza, J.R.; Winters, T.H.; Goldberg, R.

Objective:
To determine reasons why smokers are more frequently involved in motor vehicle accidents than nonsmokers.

Methods or Approach:
Questionnaires are administered to high risk and low risk populations to determine the influence of age, sex, marital status, education, driving experience, alcohol use, and tobacco use on driving record.

Results to Date:
Smokers have statistically significant increased risk of motor vehicle accidents even after controlling for alcohol consumption. Smokers also incur more moving traffic violations than nonsmokers.

Project Dates:
March 1984–March 1985.

Financial Support:
University of Massachusetts Medical Center.

1093. UNIVERSITY OF MASSACHUSETTS, MEDICAL SCHOOL, Department of Physiology, 55 Lake Avenue, North, Worchester, Massachusetts 01605.

Project Title:
Physiological Effects of Nicotine on Single Smooth Muscle Cells.

Principal Investigator:
Yamaguchi, H.

Objective:
To investigate physiological effects of nicotine on enzymatically dispersed smooth muscle cells from toad stomach to eliminate simultaneous actions of neurotransmitters released from nerve endings by nicotine, which is known to occur in intact tissue preparations.

Methods or Approach:
Electrophysiological methods are employed (fine-tipped micropipettes) to record resting membrane potentials and double-barreled Ca^{2+}-selection microelectrodes to record level and changes of ionized intracellular Ca^{2+} during application of nicotine over dispersed smooth muscle cells. The contractile state of muscle cells is assessed by video microscope and by Coulter counter cell-sizing apparatus.

Results to Date:
Nicotine depolarized resting membrane potential in a dose-dependent manner. Depolarization was accompanied by reduction of membrance resistance, suggesting that a decrease in K^+ conductance was the primary cause. However, depolarization did not result in any contraction of muscles and relaxation of smooth muscles was often observed. Degree of relaxation is greater than that induced by the β-adrenergic agonist isoproterenol at the maximum dose. Changes of intracellular Ca^{2+} are currently being investigated.

Project Dates:
July 1982–June 1985.

Financial Support:
Smokeless Tobacco Research Council, Inc.

1094. VETERAN'S ADMINISTRATION, OUTPATIENT CLINIC, 17 Court Street, Boston, Massachusetts 01208.

Project Title:
A Prospective Analysis of the Smoking Cessation Process.

Principal Investigators:
Garvey, A.J.; Heinold, J.W.

Objective:
To examine the early period after smoking cessation (during which relapse is highly probable) to determine factors associated with relapse and with maintenance of abstinence.

Methods or Approach:
Approximately 300 smokers who are attempting to quit smoking will be followed prospectively for 2 years after the cessation attempt.

Results to Date:
Project is in a preliminary phase.

Project Dates:
October 1984–October 1987.
Financial Support:
VA Medical Research Service.

1095. VETERANS ADMINISTRATION MEDICAL CENTER, 150 South Huntington Avenue, Boston, Massachusetts 02130.

Project Title:
VAOPC Psychiatric Diagnostic and Follow-Up Project—Phase I.

Principal Investigator:
Burr, W.A.
Objective:
To investigate the long-term course of nonpsychotic psychiatric disorders; study determinants of early mortality.
Methods or Approach:
The sample size will be expanded, and means will be developed of assessing smoking and alcohol use history among both living and deceased subjects. Interview protocols will be recorded, reviewed, and designed. The project should lead to improved prognostic assessment of nonpsychotic disorders, and should help outline genetic and familial factors.
Results to Date:
Data are being prepared for publication.
Financial Support:
VA.

1096. VETERANS ADMINISTRATION, CHANNING LABORATORY, 780 Longwood Avenue, Boston, Massachusetts 02115.

Project Title:
The Epidemiology of Airways Responsiveness.

Principal Investigators:
Weiss, S.T.; Sparrow, D.
Objective:
To define relationship of cigarette smoking to airways responsiveness; determine relationship of airways responsiveness to decline in lung function in adults.
Methods or Approach:
Data will be collected from a population-based, longitudinal epidemiological study.
Results to Date:
Project is in a preliminary phase.
Project Dates:
April 1984–April 1989.
Financial Support:
NHLBI (HL 32216).

1097. VETERANS ADMINISTRATION, OUTPATIENT CLINIC, 17 Court Street, Boston, Massachusetts 02108.

Project Title:
The Longitudinal and Cross-Sectional Study of Oral Health in Healthy Veterans (Dental Longitudinal Study).

Principal Investigators:
Chauncey, H.H.; Kapur, K.K.; Feldman, R.S.
Objective:
To determine incidence, distribution, changes, and interrelationships of oral variables frequently used to indicate oral health and oral disease status; elucidate mechanisms involved in oral disease processes and methods of prevention.
Methods or Approach:
Information is obtained during periodic examinations (3-year intervals) of more than 1,200 participants of the Veterans Administration Normative Aging Study. Examinations include (1) interim dental history; (2) comprehensive orofacial examination (periodontium, caries, prosthesis evaluation); (3) masticatory function tests and survey of dietary habits (preferences for taste, texture, ease of chewing, and ingestion frequency); (4) biochemical analysis of stimulated whole and parotid saliva; and (5) various general procedures (intraoral and panoramic radiographs, lateral and frontal cephalometric radiographs, diagnostic casts, and oral cytologic smears). Approximately 400 participants are recalled each year. Certain subpopulations (individuals with specific socioeconomic, psychosocial, biomedical, and health or habit backgrounds) are occasionally utilized in special surveys.
Results to Date:
Six indices of periodontal health were recorded in cigarette, pipe, and cigar smokers and in nonsmokers, including calculus deposition, plaque accumulation, gingival inflammation, periodontal pocket depth, alveolar bone loss, and tooth mobility. Cigarette smokers had significantly more calculus deposition than pipe/cigar smokers, although both groups had more than nonsmokers. Cigarette smokers accumulated slightly less plaque than pipe/cigar smokers, and both groups accumulated less than nonsmokers. Gingival inflammation and tooth mobility did not differ between smokers and nonsmokers or between smoker groups. Cigarette smokers had significantly greater pocket depth than nonsmokers, in contrast to pipe/cigar smokers who were not different from nonsmokers. Radiographic measurements indicated that cigarette smokers had significantly more alveolar bone loss than either pipe/cigar smokers or nonsmokers. After covariance adjustment for age and calculus, all smokers had less plaque, gingival inflammation, and tooth mobility than nonsmokers and similar periodontal pocket depth; however, only cigarette smokers had greater bone loss. Greater bone loss in cigarette smokers suggests a tobacco product-related effect in systemic physiologic action.
Future Plans:
Comprehensive longitudinal analyses are being conducted that should provide a description of some of the changes that occur during the normal aging process, and that should yield information relevant to certain pathological conditions.
Project Dates:
January 1969–continuing.
Financial Support:
VA.

1098. WORCESTER FOUNDATION FOR EXPERIMENTAL BIOLOGY, 222 Maple Avenue, Shrewsbury, Massachusetts 01545.

Project Title:
Gonadal Correlates of Smoking.

Principal Investigator:
Klaiber, E.L.
Objective:
To examine effects of cigarette smoking on gonadal function in adult men and women.
Methods or Approach:
Studies will be carried out in two separate populations. Serum estradiol will be measured and seminal fluid will be analyzed for 100 husbands of infertile couples. For 2[illegible] of the infertile husbands, blood metabolic clearance rate and production rate of estradiol will be measured on two occasions: prior to

smoking cessation and after 6 months of not smoking. Similar studies will be performed in a group of nonsmokers and in men who continue to smoke. Among 100 women (50 percent smokers), measurements will be made of serum estradiol, progesterone, and testosterone during pre- and postovulatory phases of the cycle to determine whether there is a higher incidence of anovulatory cycles in women who smoke than in nonsmoking women. Gonadal hormones will be measured by radioimmunoassay. Blood metabolic clearance and production rates will be determined by intravenous administration of a radioactively labeled hormone at a known constant rate until a "steady state" exists. Metabolic clearance rate is measured by dividing rate of infusion of isotopic steroids by plasma concentration of isotopic steroid. Production rate is measured by multiplying level of isotopic hormone in the blood by metabolic clearance rate. Seminal fluid analyses will measure sperm count, percent of motility, grade of motility, and percent of abnormal forms.

Results to Date:
Results to date indicate that in a population of infertile males, smoking impairs sperm count and percent and grade of motility. Serum estradiol levels were elevated in male smokers and level of serum estradiol was negatively correlated with sperm count. Women who smoke have a higher percentage of anovulatory cycles than nonsmoking women.

Project Dates:
March 1983–February 1986.

Financial Support:
NICHD (5R01HD17220-05).

Michigan

1099. AMERICAN INSTITUTE FOR PREVENTIVE MEDICINE, 19111 West 10 Mile Road, Suite 101, Southfield, Michigan 48075.

Project Title:
Study of Nicorette as a Pharmacological Adjunct to a Multiple Treatment Smoking Cessation Program.

Principal Investigator:
Powell, D.R.

Objective:
To help smokers quit by addressing the importance that both psychological and physiological components play in perpetuating smoking behavior; improve cessation rates by adding Nicorette, a nicotine chewing gum, to a multiple treatment smoking cessation program.

Methods or Approach:
All subjects will be asked to attend an introductory session during which the research project will be described. A baseline test to measure thiocyanate levels shall be administered. Subjects will receive a booklet that presents a series of assignments for them to carry out in preparation for the treatment program that begins the following Monday. These assignments include recording all cigarettes smoked, collecting cigarette butts, reading some articles about smoking, delaying smoking behavior, removing smoking paraphernalia, etc. Subjects will attend five 1-hour treatment sessions on consecutive days. Program materials and quitting techniques presented will draw upon basic behavior modification theory and will include stimulus control, stress management, nutrition awareness, attitude transformation, development of incompatible behavior, and negative smoking. The program is designed to teach subjects the necessary skills for achieving permanent smoking abstinence, including procedures for both preventing and eliminating cigarette urge sensations. On the last day of the program, subjects will be assigned to one of three posttreatment conditions: (1) Nicorette chewing gum as a posttreatment procedure; (2) placebo gum as a posttreatment procedure; and (3) a control group. Clinic visit followups will be conducted at 3, 6, and 12 months posttreatment where saliva thiocyanate tests will be administered to determine success data.

Results to Date:
To date, 6-month data for 98 subjects (less than one-half of the total number of subjects in the project) have been compiled. Results showed that (1) the group that received behavior modification plus placebo demonstrated a 42.4 percent quit rate; (2) the group that received behavior modification plus Nicorette demonstrated a 47.1 percent quit rate; and (3) the group that received behavior modification and no gum showed a 19.4 percent success rate. These findings were verified by saliva thiocyanate measures.

Future Plans:
Six-month success rates will be gathered for an additional 150 subjects and 1-year data will be gathered for all subjects. In addition, analyses will be made to compare the three treatment conditions on key demographic and smoking history information and on their responses to Fagerstrom's Smoking Tolerance Scale.

Project Dates:
January 1980–1983.

Financial Support:
Dow Chemical U.S.A.

1100. AMERICAN INSTITUTE FOR PREVENTIVE MEDICINE, 19111 West 10 Mile Road, Suite 101, Southfield, Michigan 48075.

Project Title:
Anti-Smoking Program for Coronary Prone Men: An Evaluation Study.

Principal Investigators:
Powell, D.R.; Arnold, C.B.

Objective:
To evaluate a 5-day multiple treatment smoking cessation program with participants in the National Heart, Lung, and Blood Institute's Multiple Risk Factor Intervention Trial (MRFIT).

Methods or Approach:
MRFIT was a 6-year project designed to prevent CHD mortality in middle-aged men. The subjects in the study had been resistant to previous smoking cessation efforts and were now participating and being evaluated in a new stop-smoking program. The 22 MRFIT men enrolled in the program were divided into two groups: (1) 14 men who went through the program the week following an explanatory meeting, and (2) 8 men who began 2 weeks later. All 22 attended the entire program. The Smokeless Program, which consisted of four consecutive 1.5-hour sessions held Monday through Thursday, was a highly structured multiple treatment program intended to teach skills to achieve permanent abstinence from smoking. It was based upon the assumption that quitting smoking is

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easier when specific behavioral skills are available to the ex-smoker to handle the anticipated urges and desires to smoke. The program taught well-known behavior modification and self-control techniques including stimulus control, relaxation training, thought stopping, eating management, behavioral rehearsal, and cognitive coping skills.

Results to Date:
At the end of treatment, 19 of the 22 men (86 percent) had quit smoking. At 6-month posttreatment, 13 (59 percent) were abstinent and at the end of 1 year, 11 (50 percent) were abstinent. These results were determined by serum thiocyanate measures where levels less than 100 mmol/L were used to indicate a nonsmoker. The baseline serum thiocyanate measures were altered significantly after treatment in those who quit smoking, from a pretreatment mean of 166 mmol/L to a 12-month level of 35 mmol/L. In contrast, the mean serum thiocyanate measures of the smokers remained virtually unchanged from a baseline level of 182 mmol/L.

Project Dates:
June 1979–1981.

Financial Support:
NHLBI (NOI-HV-22983).

1101. AMERICAN INSTITUTE FOR PREVENTIVE MEDICINE, 19111 West 10 Mile Road, Suite 101, Southfield, Michigan 48075.

Project Title:
Evaluation of the American Institute for Preventive Medicine's SMOKELESS System in Corporate Settings.

Principal Investigator:
Powell, D.R.

Objective:
To evaluate the American Institute for Preventive Medicine's SMOKELESS program being offered to employees of the Ford Motor Company.

Methods or Approach:
SMOKELESS is a multiple treatment approach to smoking cessation that addresses smoking behavior from behavioral, physiological, sociological, and economic perspectives. The program, which teaches participants a systematic technology for preventing and eliminating urges to smoke, is based on the philosophy that quitting is easier when one knows how to do it. SMOKELESS consists of three phases, which are all important to the quitting process; a preparatory phase that prepares smokers for quitting, a treatment phase that involves extensive training in behavior modification techniques, and a maintenance phase that reinforces nonsmoking behavior so that it remains permanent.

Results to Date:
To date, a total of 600 employees from 11 different divisions have participated in the program. The mean quit rate is 94 percent at end of treatment. Five of the divisions have been evaluated at the 6-month posttreatment point, with quit rates that ranged from 53 percent to 82 percent. Subjective participant evaluations of the program have been uniformly high. Rating the program on a scale of from 1.0 (excellent) to 5.0 (poor), participants' mean rating was 1.47.

Future Plans:
All participants will be followed through 12-month posttreatment evaluation. The program will be offered to other divisions.

Project Dates:
September 1983–September 1987.

Financial Support:
American Institute for Preventive Medicine.

1102. MICHIGAN MOLECULAR INSTITUTE, 1910 West St. Andrews, Midland, Michigan 48640.

Project Title:
Specificity of BaP Diol Epoxide Binding to DNA.

Principal Investigators:
Meehan, T.; Becker, J.F.; Yamamoto, J., et al.

Objective:
To investigate (1) the role of intercalation in the binding of benzo(*a*)pyrene (BaP) diol epoxide to DNA by spectral analysis of physical complexes and the kinetics of their formation; (2) possible sequence-specific covalent binding by use of DNA sequencing techniques; (3) mutagenesis mechanisms by replicating hydrocarbon-modified DNA in vitro and sequence analysis of the newly synthesized strand; and (4) the relevance of DNA covalent adducts to the biological properties of BaP by analyzing in vivo adducts from target (skin) and nontarget (liver) tissues.

Methods or Approach:
To understand the asymmetric interactions between BaP and DNA, the activated form of the carcinogen BaP, $(\pm)7\beta,8\alpha$-dihydroxy-$9\alpha,10\alpha$-epoxy-7,8,9,10-tetrahydrobenzo(*a*)pyrene (($\pm$)anti-BaP diol epoxide), has been synthesized and it has been determined through fluorescence, absorbance, and circular dichroism spectroscopy and high resolution mass spectrometry that the hydrocarbon reacts to form a pair of diastereomers with the exocyclic amino groups of deoxyguanosine, deoxyadenosine, and probably deoxycytidine in DNA. This reaction is stereoselective for guanine in double-stranded DNA but not with single-stranded polydeoxynucleotides or with monodeoxynucleotides. Physical interactions between the hydrocarbons and DNA prior to alkylation may play a role in asymmetric covalent binding. By comparing relative repair rates in target (skin) and nontarget (liver) tissues, in addition to adduct analysis, information on the biological relevance of BaP-DNA alkylation products may be provided. Currently, any sequence specificity in the covalent binding of BaP diol epoxide to DNA, and the molecular mechanisms of mutation caused by covalent binding of the hydrocarbon to DNA, are being investigated.

Results to Date:
It has been found that the BaP diol epoxide forms a physical complex with DNA. This complex has been characterized by spectroscopic analysis and the measurement of superhelical DNA unwinding angles. The results of these studies indicate that the hydrocarbon forms a physical complex with DNA by interrelating between the stacked base pairs of the helix. Also investigated were the kinetics of formation of the complex, utilizing temperature-jump techniques. The physical complex forms on an MS time scale. Under the same conditions, the BaP diol epoxide covalently binds to DNA on a time scale of minutes. Thus, it is proposed that physical complex formation between the hydrocarbon and DNA takes place prior to covalent attachment.

Project Dates:
August 1979–continuing.

Financial Support:
NCI (1RO1CA25106); Michigan Molecular Institute.

1103. UNIVERSITY OF MICHIGAN, Department of Postgraduate Medicine, Box 057, Ann Arbor, Michigan 48109.

Project Title:
Peer Pressure in Recruitment to Cigarette Smoking.

Principal Investigators:
Dielman, T.E.; Horvath, W.J.
Objective:
To (1) test the effectiveness of a role-playing preventive health behavior intervention with fifth and sixth grade children in reducing the recruitment to cigarette smoking during the junior high school years; (2) test the relative effectiveness of a 1-year and 2-year exposure to the intervention; (3) test sex differences in responsiveness to the intervention; (4) test the relationship of measures of self-esteem and locus of control to cigarette smoking; and (5) test the relative effectiveness of the intervention among children who score high and low on measures of self-esteem and locus of control.
Methods or Approach:
A series of four intervention sessions was conducted with an experimental group of fifth and sixth graders in two school systems during year 1, while a control group received no intervention. Both groups received pre- and posttests. During year 2 some of the experimental group received a series of three "booster" sessions in the sixth grade. All students were pre- and posttested in the second year, including those who had progressed to junior high school. In addition, seventh graders who were not in the study during the first year were pre- and posttested in the second year.
Results to Date:
Results indicate that intervention was effective in deterring experimentation with cigarettes for boys, but not for girls, in the two school systems. The intervention was effective in deterring onset of more frequent smoking for both sexes in the first school system, but only for boys in the second system. There was no generalizability of the prevention program to deterrence of alcohol or marijuana use. Implementation of the prevention program in the fifth grade with a series of booster sessions in the sixth grade was no more effective than implementation in the sixth grade with no booster sessions. Measures of self-esteem and locus of control were related to adolescent health behavior, but were not influenced by the program. Levels of locus of control and self-esteem did not interact significantly with exposure to the program in deterring adoption of detrimental health behaviors.
Project Dates:
August 1980–July 1983.
Financial Support:
NIDA (DA02644).

1104. UNIVERSITY OF MICHIGAN, INSTITUTE FOR SOCIAL RESEARCH, Survey Research Center, Box 1248, Ann Arbor, Michigan 48106.

Project Title:
Monitoring the Future: A Continuing Study of the Lifestyles and Values of Youth.

Principal Investigators:
Johnston, L.D.; Bachman, J.G.
Objective:
To assess the changing lifestyles, values, and preferences of American youth, including smoking behavior (past and present) and attitudes about smoking and its risks.
Methods or Approach:
The Monitoring the Future project involves a series of annual, nationwide questionnaire surveys of seniors in high schools, which began with the class of 1975, and annual followup surveys mailed to a subset of each sample for up to 10 years following their graduation. Thus, the population of interest consists of most young American men and women, in the age range of approximately 18-28 years, monitored through an ongoing series of cohort analyses. Data collection takes place in approximately 130 public and private high schools selected to provide an accurate cross-section of high school seniors throughout the United States. The procedure for securing this sample includes the selection of particular geographic areas, selection of one or more high schools in each area, and selection of seniors within each high school. The issues addressed are broad in scope: views about personal lifestyles, confidence in social institutions, intergroup and interpersonal attitudes, concerns about conservation and ecology, behaviors and attitudes related to drug use, and other social and ethical issues. A major emphasis is placed on drug use and attitudes about drugs. Drug topics include smoking behavior (past and present) and attitudes about smoking and its risks.
Results to Date:
It appears that 1976 and 1977 were the peak years for lifetime, annual, and daily prevalence of cigarette smoking. Over the subsequent four graduating classes (1978-1981), daily cigarette use dropped from 29 percent to 20 percent, and daily use of a half-pack or more decreased from 19.4 percent to 13.5 percent. However, since 1981, smoking rates among high school seniors have remained stable. Females show a slightly higher rate of heavy smoking (half-pack a day or more) than males (13.6 percent versus 13.1 percent); they also are more likely to be occasional but not regular smokers (17.7 percent versus 14.9 percent). Smoking is very strongly related to college plans. The proportion of the non-college-bound seniors who currently smoke half-a-pack or more daily is almost three times as great as the proportion of the college-bound (20.9 percent versus 7.6 percent). There are also large regional differences in regular smoking: daily rates of half-a-pack a day (or more) are more than twice as high in the Northeast (16.6 percent) and North Central (17.1 percent) regions as in the West (6.4 percent). The South has an intermediate rate of 12.4 percent. Practically no current smokers are resigned to the fact that their habits will continue, since only 1.4 percent of the sample say they will "definitely" be smoking 5 years in the future. There was a gradual, but important, increase between 1975 and 1981 in the proportion of seniors who thought pack-a-day smoking involves great risk for the user (from 51 percent in 1975 to 63 percent in 1981). Since 1981, this figure has declined slightly, to 61 percent in 1983. Between 1975 and 1981, there was also an increase in the proportion of seniors saying that their friends would disapprove of their smoking a pack a day (from 64 percent in 1975 to 74 percent in 1981). After 1981, this percentage also dropped slightly, to 72 percent in 1983. (Declines are not statistically significant.) Fully 41 percent of the most recent class believe that cigarette smoking in public places should be prohibited by law.
Future Plans:
The design calls for systematic monitoring of attitudes, plans, and behaviors of American youth on a continuing annual basis.
Project Dates:
June 1975–continuing.
Financial Support:
NIDA (DA-01411).
References:
(1) Johnston, L.D.; Bachman, J.G.; O'Malley, P.M. *Highlights From Student Drug Use in America, 1975-1981.* Washington, D.C., U.S. Government Printing Office, 1981, 130 pp. (2) Johnston, L.D.; Bachman, J.G.; O'Malley, P.M. *Student Drug Use in America, 1975-1981.* Washington, D.C., U.S. Government Printing Office, 1982, 450 pp. (3) Johnston, L.D.; O'Malley, P.M.; Bachman, J.G. *Highlights From Drugs and American High School Students, 1975-1983.* U.S. Government Printing Office, 1984, 135 pp. (4) Johnston, L.D.; O'Malley, P.M.; Bachman, J.G. *Drugs and American High School*

Students, 1975-1983. U.S. Government Printing Office, 1984, 481 pp.

1105. UNIVERSITY OF MICHIGAN, SCHOOL OF PUBLIC HEALTH, Department of Epidemiology, 109 South Observatory, Ann Arbor, Michigan 48109.

Project Title:
Passive Smoking, Respiratory Symptoms, Lung Function, and Initiation of Smoking in Tecumseh, Michigan. (Doctoral Dissertation).

Principal Investigators:
Burchfiel, C.M.; Higgins, M.W.; Higgins, I.T.T., et al.

Objective:
To (1) investigate the relationship between passive exposure to household cigarette smoke, prevalence of respiratory conditions, and lung function in a defined pediatric population; (2) identify baseline characteristics that predict initiation of smoking; and (3) assess the relative contribution of variables that may potentially confound these relationships.

Methods or Approach:
Cross-sectional and longitudinal (over a 15-year period) designs were used to determine whether prevalence and incidence of respiratory conditions, level and change in pulmonary function, and initiation of smoking were related to parental smoking habits. More refined measures of passive smoking were developed, including number of parental smokers during a child's lifetime, total number of household smokers, and amount and duration of parental smoking. Logistic regression models were employed for dichotomous outcome variables. Lung function was adjusted for age and height and expressed as a percent of predicted or in units of volume or flow derived from an analysis of covariance model.

Results to Date:
Several respiratory conditions at baseline and followup were significantly related to parental smoking for 3,482 nonsmoking children aged 0 to 19 years in 1962-1965. Most associations remained significant when parental education, family size, active smoking, and parental history of respiratory conditions were taken into account. Lung function was generally lower for those passively exposed to cigarette smoke at baseline. Offspring of parents who smoke were significantly more likely to initiate smoking than offspring of parents who never smoked.

Project Dates:
September 1980–April 1984.

Financial Support:
University of Michigan.

1106. UNIVERSITY OF MICHIGAN, SCHOOL OF PUBLIC HEALTH, Department of Health Behavior and Health Education, Ann Arbor, Michigan 48109.

Project Title:
Effect of a Minimal-Contact Smoking Cessation Program in a Health Care Setting.

Principal Investigators:
Strecher, V.J.; Becker, A.H.; Kirscht, J.P., et al.

Objective:
To evaluate the effect of a minimal-contact smoking cessation program (brief practitioner consultation, self-help manual, and incentive to comply with manual) for inpatients and outpatients at a Veterans Administration Medical Center by degree of acceptability and effectiveness; examine the role of psychosocial factors (health beliefs, self-efficacy, anxiety, social support) on future ability to quit smoking.

Methods or Approach:
During an inpatient or outpatient visit to the medical center, veterans received a questionnaire and were enrolled in a smoking cessation intervention trial, some receiving practitioner-initiated minimal-contact intervention and the others usual care. Smoking status was assessed 3 months following hospital discharge. Enrollment procedures differed from those of many other smoking intervention trials in that, rather than recruiting only those who were motivated to respond to an announcement of program availability, all patients who smoked and would normally be considered eligible for a smoking cessation program were actively sought.

Results to Date:
The program had a high degree of acceptance by patients who smoked; over 60 percent agreed to participate and take home the self-help smoking cessation manual. The approach was effective in getting patients to reduce daily consumption, with some patient groups exhibiting higher cessation rates than others. Analyses of questionnaire data revealed that patients most likely to have reduced smoking, whether in the intervention or control group, were those reporting both high perceived susceptibility and high expectations of efficacy. Those least likely to have reduced smoking were those reporting high susceptibility but low efficacy, what has been characterized as a "learned helplessness" mode.

Future Plans:
Results will be prepared for publication, and the effect of the program in different hospitals with different health practitioners will be explored.

Project Dates:
August 1982–1985.

Financial Support:
University of Michigan; VA; NHLBI.

1107. UNIVERSITY OF MICHIGAN, Department of Pharmacology, M6414 Medical Science Building I, Ann Arbor, Michigan 48109-0010.

Project Title:
Effect of Nicotine and Related Substances on the Central Nervous System.

Principal Investigator:
Domino, E.F.

Objective:
To determine effects of constituents of tobacco smoke on the central nervous system.

Methods or Approach:
Neurophysiological and neurochemical methods will be used to determine effects.

Results to Date:
Nicotine, in amounts absorbed during smoking and in toxic amounts, produces profound effects on the central nervous system.

Project Dates:
January 1984–continuing.

1108. VETERANS ADMINISTRATION MEDICAL CENTER, 2215 Fuller Road, Ann Arbor, Michigan 48105.

Project Title:
Life Change Events as a Predictor of Success in Stop Smoking Clinics.

Principal Investigator:
Gunn, R.C.

Objective:
To test the hypothesis that smoking cessation in a Stop Smoking Clinic is related to reporting a low amount of current stress on a Life Change Scale; establish whether increasing age and amount smoked would be effective predictors of being unable to stop smoking at the Clinic.

Methods or Approach:
Participants ($n = 231$) voluntarily attending 1 of 17 American Cancer Society California model Stop Smoking Clinics (8 sessions), filled out a smoking history questionnaire and a Life Change Scale, an 11-item condensed version of Holmes and Rahe's Social Readjustment Rating Scale. Subjects simply checking two or less life changes in the last 3 months were classified as under low life stress; those scoring three or more changes, under high life stress. Clinic success was based on subjects' reports at the final session of having stopped smoking (the third session was a cold turkey quit day). A total of 101 people finished the Clinic, with 87 reporting having stopped smoking.

Results to Date:
In the total group, life stress did not relate to stopping smoking. However, when low and high life stress groups were compared by sex, high scores strongly predicted males ($n = 88$) failing to stop ($p < 0.005$). Life stress scores did not predict females' ($n = 143$) ability to stop. Age (equivalent to length of time smoking) and daily amount smoked before Clinic attendance predicted stopping in women, but not in men. Older women stopped less frequently than younger females ($p < 0.01$), and younger women who smoked less had a high rate of success ($p < 0.05$).

Future Plans:
Further research is planned to identify why the males who attend Stop Smoking Clinics are more susceptible to life stress than women. Alternate treatments for high-stressed males wishing to stop smoking will be devised and tested.

Project Dates:
March 1980–1982.

Financial Support:
VA.

Reference:
Gunn, R.C. "Smoking Clinic Failures and Recent Life Stress." *Addictive Behaviors* 8:83-87, 1983.

1109. VETERANS ADMINISTRATION MEDICAL CENTER, 2215 Fuller Road, Ann Arbor, Michigan 48105.

Project Title:
Measuring Personal Health Risk From Smoking in Heavy, Light and Former Cigarette Users.

Principal Investigator:
Gunn, R.C.

Objective:
To test the hypothesis that many smokers deny to themselves any personal vulnerability, using a projective test instrument designed to measure such subjective vulnerability.

Methods or Approach:
Outpatient male veterans will be divided into three groups: (1) 60 light smokers, (2) 60 heavy smokers, and (3) 60 ex-smokers. Subjects will answer demographic questions, will take a short survey of knowledge about the ill effects of smoking, and will be administered the projective Smoking Story Test. Personal vulnerability will be measured by the amount of physical damage from smoking reported by story characters. It is expected that light and ex-smokers will report considerably more negative health outcomes than heavy smokers regardless of smoking danger knowledge claimed in the opinion survey. Such a result might suggest that educational campaigns discouraging smoking will have the most effect if smokers can be made to sense a personal health risk rather than receiving further factual information about the dangers of smoking.

Results to Date:
Heavy smokers still tend to deny a link between smoking and cancer, heart disease, and general health. Smokers reported no less personal vunerability on the projective test than ex-smokers; thus, the major hypothesis was not supported. Smokers clearly gave more responses on the projective test that were scored "oral" than ex-smokers, even when amount of alcohol subjects claimed to use was controlled, suggesting that smoking is a highly "oral" psychological event.

Project Dates:
May 1984–December 1984.

Financial Support:
VA.

1110. VETERANS ADMINISTRATION MEDICAL CENTER, 2215 Fuller Road, Ann Arbor, Michigan 48105.

Project Title:
Does Living With Smokers Make Quitting Cigarettes More Difficult?

Principal Investigator:
Gunn, R.C.

Objective:
To (1) examine stopping process issues for people voluntarily attending stop smoking clinics; (2) determine whether success at a clinic is related to living with smokers or nonsmokers; (3) establish whether housemates' interest affects ability to quit; and (4) investigate interactions between the variables.

Methods or Approach:
Subjects (147 people who attended several American Cancer Society Stop Smoking Clinics), completed a brief questionnaire about smoking history and habits and demographic information before starting the clinic. Participants were asked specifically with whom they currently lived, their relationship to those persons, whether or not their housemates smoked and, marking on a scale, how interested they believed the housemates were in their quitting smoking. Smoking status at clinic's end was based on self-report and leaders' observations.

Results to Date:
Chances of stopping smoking were not enhanced by living either with nonsmokers or with people believed to have high interest in one's stopping, regardless of how close the relationship was. Giving up a smoking addiction seems to require inner motivation from the smoker, with external cues for smoking and support having minimal influence in a stop smoking clinic program.

Reference:
Gunn, R.C. "Does Living With Smokers Make Quitting Cigarettes More Difficult?" *Addictive Behaviors* 8:429-432, 1983.

1111. WAYNE STATE UNIVERSITY, SCHOOL OF MEDICINE, 540 East Canfield Avenue, Detroit, Michigan 48201.

Project Title:
Nicotine-Induced Alterations in Blastocyst Development and Uterine Function in the Rat.

Principal Investigator:
Mitchell, J.A.

Objective:
To obtain a greater understanding of the means by which nicotine modifies uterine function, embryo development, and consequently the process of implantation.

Methods or Approach:
The effects of various doses of nicotine on embryo growth are determined by counting nuclei of embryos retrieved at selected times prior to implantation from control vs. nicotine-treated rats. The effect of the alkaloid on oviductal and uterine blood flow are determined by Rb^{86} fractionation; alteration in intrauterine oxygen tension is determined in vivo by micro O_2 electrode techniques. The effects of nicotine on plasma levels of gonadotropin and ovarian steroid hormones are also determined.

Results to Date:
Nicotine administration modified the rate of embryo growth as evidenced by (1) delay in the time of zona pellucida loss; (2) delay in the rate of inner cell mass growth; and (3) delay in the rate of cell proliferation. Nicotine also delays the mean time of parturition by approximately 7.5 hours and alters the mean time of onset of delivery. However, it does not exert adverse effects on litter size, sex distribution, mortality rate, or birth weight. Embryo growth is susceptible to the growth-suppressing effects of nicotine while residing within the oviduct. The conceptus is vulnerable to the growth-suppression effect of nicotine at the 2-4 cell stage of division. Preliminary studies indicate that a single injection of nicotine in early pregnancy is sufficient to result in a persistent retardation in embryo growth. The growth-suppressing effects of nicotine are probably a result, in part, of a marked and sustained reduction in oviductal and uterine blood flow which curtails the availability of oxygen and essential nutrients required for optimal embryo growth. Appropriate doses of serotonin mimic selected nicotine effects on the reproductive tract, i.e., result in comparable reductions in oviductal and uterine blood flow and in reduced uterine responsivity to decidualization. However, unlike nicotine, serotonin is highly embryotoxic.

Project Dates:
January 1981-1984.

Financial Support:
CTR (1351).

1112. WAYNE STATE UNIVERSITY, Room 160, Old Main, Detroit, Michigan 48202.

Project Title:
Peer Influence on Adolescent Cigarette Smoking.

Principal Investigator:
Urberg, K.

Objective:
To test a theoretically based model of peer influence on adolescent cigarette smoking.

Methods or Approach:
Theoretical basis was provided by social learning theory, Health Belief model, and Ajzen and Fishbein's Behavioral Intervention model. A questionnaire was administered to approximately 400 ninth grade students to ascertain individual smoking habits, perceptions of peer smoking, attitudes about smoking, perceived vulnerability to health effects of smoking, value placed on peer affiliation, and perceived pressure from friends to smoke. Path analytic techniques and analysis of variances were used to analyze data.

Results to Date:
Results confirmed most of the proposed model pathways. There were significant pathways from peer smoking to perceived peer pressure, perceived vulnerability, and attitudes about smoking. There were also significant pathways from attitudes and perceived vulnerability to smoking. The pathway from perceived peer pressure to smoking was significant only in adolescents who placed a high value on peer affiliation.

Project Dates:
September 1981–January 1983.

Financial Support:
Wayne State University.

1113. WAYNE STATE UNIVERSITY, Department of Family and Community Resources, Room 160, Old Main, Detroit, Michigan 48202.

Project Title:
Adolescent Cigarette Smoking: Pathways of Peer Influence.

Principal Investigators:
Urberg, K.A.; Liang, J.

Objective:
To (1) specify pathways by which peers may influence adolescents to begin and/or maintain cigarette smoking; (2) apply model to data derived from adolescent population; (3) determine relative contribution of designated pathways of peer influence; and (4) determine if relative contribution is similar in subgroups that differ according to age, sex, value of peer affiliation, or stage of smoking.

Methods or Approach:
Research will use a cross-sectional design. Data will be collected from 2,500 adolescents in 8th and 11th grade. Sex, race, and socioeconomic status are demographic variables of interest. Saliva samples will be collected to increase validity of self-reported smoking.

Results to Date:
Project is in a preliminary phase.

Project Dates:
May 1985–April 1988.

Financial Support:
NICHD.

1114. CALIFORNIA SCHOOL OF PROFESSIONAL PSYCHOLOGY, Human Services, Inc., 7066 Stillwater Boulevard, North, Oakdale, Minnesota 55119.

Project Title:
A Predictive Model of Outcome Differences Between Self-Treatment and Program Treatment Subjects.

Principal Investigator:
Wojcik, J.
Objective:
To investigate the impact of different values and beliefs on successful cessation of smoking; determine differences in values and beliefs of persons entering treatment programs compared with people who quit without entering a treatment program.
Methods or Approach:
Participants (n=75) in six central California smoking treatment programs and 75 persons who quit without attending such a program filled out questionnaires. All subjects quit in December 1983 or January 1984 and were followed up after 3 months. Abstinence was corroborated by family members or roommate. Questionnaires were designed to reflect a model of health-promoting behavior based on the Social Learning Theory concepts of health and general locus of control, health valuing, and self-efficacy. Data were analyzed using stepwise discriminant function techniques for groups of program treatment relapsers, program treatment abstainers, self-treatment relapsers, and self-treatment abstainers.
Results to Date:
Comparison of all abstainers to all relapsers showed self-efficacy to be the best predictor of continued abstinence. Higher health valuing predicted relapse, and higher attribution to others of power over their health predicted both the use of a treatment program and relapse. Self-treatment abstainers were most different from self-treatment relapsers, with 25 percent of the variance accounted for on the first function. This group of abstainers was higher in self-efficacy, lower in ranked valuing of health, and lower in attribution to others of power over their health.
Future Plans:
Data on 9-month followup will be analyzed to compare changes over time.
Project Dates:
June 1983–January 1985.

1115. MAYO FOUNDATION, 200 First Street, Rochester, Minnesota 55905.

Project Title:
Effect of Cigarette Smoking on Carotid Artery Atherosclerosis.

Principal Investigators:
Whisnant, J.P.; Baker, H.L., Jr.
Objective:
To determine whether there is a correlation between extent of cigarette smoking and degree of atherosclerotic lesions in the carotid artery in the cervical region or in the intracranial region.
Methods or Approach:
Patients who have cervical-cerebral arteriography will be selected in 12 age-sex groups (from age 40 through 69). Each patient who has an arteriogram during the period of acquisition will have a smoking history taken prior to the study (duration of smoking, average number of cigarettes/day, and peak number of packs). If the patient has stopped smoking, similar information will be obtained in addition to the year when smoking was stopped. In reviewing arteriographic studies, the presence or absence of atherosclerotic lesions is recorded at each of two sites in the extracranial carotid and two sites in the intracranial internal carotid. Each individual will be assigned a "stenosis score" (equal to the average of the maximal stenosis near the carotid bifurcation on both sides) recorded as the value of the midpoint of the atherosclerosis class in which the patient is classified on each side. Multiple regression analysis will be performed in which the stenosis score is the dependent variable and smoking (measured in terms of pack years) is the primary independent variable, permitting evaluation of other risk variables as influencing the stenosis score and also permitting determination of the effect of smoking after adjusting for other variables.
Results to Date:
About 400 patients have been recruited and smoking histories have been obtained. Data have not been analyzed.
Financial Support:
NIH.

1116. MAYO MEDICAL SCHOOL, Mayo Clinic, Rochester, Minnesota 55905.

Project Title:
Cigarette Smoking and Survival of Patients With Coronary Artery Disease.

Principal Investigator:
Vlietstra, R.E.
Objective:
To evaluate whether stopping smoking influences myocardial infarction and mortality rates of patients with angiographically proven coronary artery disease.
Methods or Approach:
The study is a spinoff of the NHLBI CASS study in which more than 20,000 arteriogrammed patients have been prospectively followed since 1975. Annual status and risk factor exposure is assessed by trained interviewers.
Results to Date:
Infarct and mortality rates, corrected for other known risk variables, are substantially lower in those entry-smokers who have been able to quit in followup. The lower mortality rates for quitters are evident in both low- and high-risk categories of medically treated patients but are less evident in surgical patients.
Future Plans:
Completion of analysis of 5-year followup is pending.
Project Dates:
January 1981–1983.
Financial Support:
NHLBI (HV-32984).
References:
(1) Vlietstra, R.E. "Risk Factors and Angiographic Coronary Artery Disease: A Report from the Coronary Artery Surgery Study (CASS)." *Circulation* 62:254-261, October 1980. (2) Vlietstra, R.E. "Factors Affecting the Extent and Severity of Coronary Artery Disease in Patients Enrolled in the Coronary Artery Surgery Study (CASS)." *Arteriosclerosis* 2:208-215, 1982.

1117. UNIVERSITY OF MINNESOTA, COLLEGE OF BIOLOGICAL SCIENCES, Department of Biochemistry, St. Paul, Minnesota 55108.

Project Title:
Biochemical Studies on the Pathogenesis of Emphysema.

Principal Investigators:
Liener, I.E.; Padmanabhan, R.; Rao, G.S.

Objective:
To evaluate the relative significance of elastolytic activity in the pathogenesis of emphysema associated with cigarette smoking; design delivery systems of inhibitors of elastase to the lungs as a therapeutic approach for the treatment of emphysema.

Methods or Approach:
Since the elastases produced by leukocytes and by alveolar macrophages are known to differ in properties, the relative contribution of leukocytes and alveolar macrophage elastase activities to the total elastolytic activity will be studied in the lung tissue of animals exposed to cigarette smoke. Rats will be exposed to cadmium aerosols and cigarette smoke, and a time study will be made of the lung lavage fluid with respect to the relative number of leukocytes and macrophages and accompanying elastase activity in the presence and absence of specific inhibitors. These animal models will be used to test the effectiveness of drug delivery systems containing specific inhibitors in the prevention of emphysema.

Results to Date:
The lungs of rats exposed to cadmium aerosols display a biphasic influx of leukocytes and macrophages in that sequence which is accompanied by an elastase activity due to a serine proteinase followed by more prolonged elastase activity attributable to a metalloproteinase. Emphysematous lesions induced in the lungs of hamsters by the intratracheal administration of elastase are effectively prevented by the intravenous or intratracheal administration of human albumin microspheres to which a specific peptide inhibitor of elastase has been covalently attached.

Future Plans:
In addition to delivery systems involving microspheres to which peptide inhibitors have been attached, the feasibility of using liposomes containing encapsulated inhibitors of leukocyte and macrophage elastases will be tested in suitable animal models. Various antioxidants will also be conjugated to microspheres or incorporated into liposomes to test their effectiveness in preventing smoke-induced emphysema in animal models.

Project Dates:
December 1977–continuing.

Financial Support:
NHLBI (HL 14865).

Reference:
Padmanabhan, R.V.; Gudapaty, S.R.; Liener, I.E., et al. "Elastolytic Activity in the Lungs of Rats Exposed to Cadmium Aerosolization." *Environmental Research* (In press).

1118. UNIVERSITY OF MINNESOTA, Department of Psychiatry, Box 393 Mayo, 420 Delaware Street, SE., Minneapolis, Minnesota 55455.

Project Title:
Nicotine Withdrawal and Smoking Treatment Outcome.

Principal Investigators:
Hatsukami, D.; Pickens, R.W.

Objective:
To (1) determine reliable, sensitive, and clinically applicable indicators of nicotine withdrawal; (2) employ these indicators in determining the relationship between the severity of nicotine withdrawal symptoms and smoking treatment success; and (3) determine how environmental stimuli are related to severity of tobacco abstinence symptoms.

Methods or Approach:
In the first phase of the study, 25 subjects were hospitalized for 7 days on a research ward. Each subject had undergone 1 day of adaptation, 2 days of baseline ad lib smoking, and 4 days of tobacco abstinence. The battery of tests administered to the subjects over the time of the hospital stay included physiological, subjective, and behavioral measures. Phase Two employs the most sensitive withdrawal indicators found in the aforementioned study to examine the relationship between nicotine withdrawal and smoking treatment outcome. Treatment outcome is related to incidence and severity of withdrawal symptoms found during an initial standard test period. In addition, the incidence and intensity of withdrawal symptoms observed during treatment will be compared between two treatment approaches (gradual vs. abrupt cessation) and related to treatment outcome.

Results to Date:
Results from the first phase showed significant effects of tobacco withdrawal in 9 of 37 symptoms previously attributed to withdrawal, including (1) decreased heart rate, (2) increased caloric intake, (3) increased weight, (4) increased reports of craving for tobacco; (5) increased confusion score as measured by the POMS; (6) increased depression–dejection score as measured by the POMS; (7) increased number of awakenings; (8) increased duration of awakenings during the sleep period; and (9) increased poor concentration as observed by the nursing staff. Only craving for cigarettes was correlated with nicotine and cotinine blood levels. Results from the second phase are undergoing analysis and the third phase is in a preliminary stage.

Future Plans:
Subjects will also be administered tests to measure abstinence symptoms in situations frequently associated with smoking behavior and in situations not frequently associated with smoking. By comparing the intensity and time course of abstinence symptoms in the two situations, the extent to which behavioral and pharmacological factors are involved in determining the severity of tobacco withdrawal symptoms will be examined.

Project Dates:
July 1981–August 1985.

Financial Support:
NIDA (2M01RR00400-16).

1119. UNIVERSITY OF MINNESOTA, Department of Medicine and Physiology, 435 Delaware Street, SE., Minneapolis, Minnesota 55455. VETERANS ADMINISTRATION MEDICAL CENTER, Minneapolis, Minnesota.

Project Title:
Aerosol Clearance May Not Measure Epithelial Permeability in Injured Lungs.

Principal Investigators:
Hertz, M.I.; Wangensteen, O.D.; Hoidal, J.R., et al.

Objective:
To investigate whether alveolar surface area and the volume of fluid on the alveolar surface influence clearance of ^{99m}Tc-diethylenetriamine-pentacetate (DTPA) in an animal model of lung injury.

Methods or Approach:
Syrian golden hamsters (100 to 150 g) were exposed (or sham-exposed) to cigarette smoke for 15 minutes, six times/day, six days/week for 6 to 12 weeks. One group of smoke-exposed animals was given 20 units of purified porcine elastase 24 hours prior to clearance and permeability measurements. All animals were anesthetized with an intraperitoneal injection of pentobarbital (50 mg/kg). Clearance of ^{99m}Tc-DTPA was measured by the radioaerosol method, and alveolar permeability and resident lung fluid volume (V_{RLF}) measurements were made using the isolated perfused lung method.
Results to Date:
Rates of ^{99m}Tc-DTPA clearance in smoke-exposed and in smoke and elastase-exposed animals were not significantly different from controls. However, the PS of ^{99m}Tc-DTPA was markedly increased in smoke and elastase-exposed animals compared with controls. Thus, increased alveolar permeability may occur that is not measurable by the radioaerosol clearance method, a discrepancy that may be explained by an increase in volume of resident lung fluid after lung injury. This would decrease the ^{99m}Tc-DTPA concentration in alveolar fluid and could result in a normal clearance rate of the tracer, even with increased permeability. In smoke- and elastase-exposed animals, an indirect measurement of resident lung fluid correlated linearly with ^{99m}Tc-DTPA. It is concluded that changes in observed pulmonary clearance of radioaerosols can reflect alterations either in epithelial permeability, volume of resident lung fluid, or both.
Financial Support:
Minnesota Medical Foundation; VA; NIH.

1120. UNIVERSITY OF MINNESOTA, 611 Beacon Street, SE., Minneapolis, Minnesota 55455.

Project Title:
Minnesota Heart Health Program.

Principal Investigator:
Blackburn, H.W.
Objective:
To understand trends in cardiovascular disability, illness, and death by surveying and analyzing measurable aspects of risk behavior, socioeconomic indicators, risk characteristics, and disease experience within a defined geopolitical area.
Methods or Approach:
The Minnesota Heart Health Program (MHHP) is a community-based research demonstration of the effect of multiple educational strategies to encourage more healthy behavior, prevent cardiovascular diseases, and promote health, based on the important demonstrated influence of blood pressure, blood lipids, and cigarette smoking on risk and the effect of mass health behaviors on population levels of these factors. Educational strategies include (1) direct "hands-on" education; (2) professional education to enhance prevention services; (3) organization and training of community leaders; (4) mass communications; and (5) enhanced community support for healthy behavior. The MHHP is designed to demonstrate new and important issues for the future of preventive efforts in public health.
Results to Date:
Results are not yet available.
Project Dates:
July 1980–July 1990.
Financial Support:
NHLBI (5R01HL25523-05).

1121. UNIVERSITY OF MINNESOTA, SCHOOL OF PUBLIC HEALTH, 1115 Mayo Building, Minneapolis, Minnesota 55455.

Project Title:
Cadmium Toxicity in Lung Cell Culture Systems.

Principal Investigator:
Stevens, J.B.
Objective:
To (1) determine sensitivity of the type II epithelial cell in primary culture to $CdCl_2$ and CdO; (2) compare results with those previously found with cultured pulmonary alveolar macrophages; and (3) determine if CdO toxicity is due to Cd^{2+} poisoning, an alkali burn, or a combination of both mechanisms.
Methods or Approach:
Type II epithelial cells are isolated by elastase-mediated tissue digestion followed by differential plating. Cytotoxicity is assessed by cell viability (dye exclusion), cell morphology (STEM), cell respiration (O_2 uptake), and cell function (dipalmitoylphosphatidylcholine synthesis). Pulmonary surfactant is isolated by differential centrifugation, and analysis of phospholipids and neutral lipids by liquid chromatography and gas chromatography.
Results to Date:
Type II epithelial cells were isolated at >80 percent purity and viability (>95 percent). Pulmonary surfactant was isolated to purity, with compositional and functional properties equal to those reported by other investigators. CdO toxicity toward macrophages in a highly buffered culture medium was identical to $CdCl_2$ toxicity. CdO toxicity toward macrophages in an unbuffered culture medium was greater than either $CdCl_2$ or NaOH alone.
Future Plans:
Futher studies will determine sensitivity of bronchiolar cell types toward $CdCl_2$ and CdO and compare data with results with macrophages and type II epithelia.
Project Dates:
July 1984–June 1986.
Financial Support:
University of Minnesota, School of Public Health.

1122. UNIVERSITY OF MINNESOTA, Division of Epidemiology, Stadium Gate 20, Minneapolis, Minnesota 55403.

Project Title:
Minnesota D-Day: Quit Smoking Contest.

Principal Investigators:
Pechacek, T.; Blake, S.; Klepp, K.-I.
Objective:
To assess prospectively the process of smoking cessation; identify factors predictive of cessation relapse or maintenance.
Methods or Approach:
Questionnaires were mailed to a sample of people who signed up for the D-Day, Quit Smoking Contest (prior to D-Day, which was identified as the official day to quit smoking). Smoking history, demographic information, and intentions and expectations about quitting smoking were evaluated prior to the contest. Phone interviews were conducted 4 months later to determine success rates for cessation, factors related to relapse or smoking "slips," and coping strategies used during high risk for smoking situations.
Results to Date:
Results are not yet available.

Project Dates:
June 1983–June 1985.
Financial Support:
Biomedical Research Support Grant.

1123. UNIVERSITY OF MINNESOTA, Division of Biometry, Suite 508, 2829 University Avenue, SE., Minneapolis, Minnesota 55414.

Project Title:
Chronic Obstructive Pulmonary Disease Prevention Trial - Data Coordinating Center.

Principal Investigators:
Kjelsberg, M.; Connett, J.
Objective:
To determine whether intervention to encourage cessation of cigarette smoking and daily use of bronchodilators can slow the decline in pulmonary function (forced expiratory volume in 1 sec, FEV_1) in smokers aged 35 to 55 who have mildly impaired pulmonary function prior to entry into the study.
Methods or Approach:
In the randomized clinical trial, eligible participants will be randomly assigned to either a control group or an intervention group. Intervention will consist of either extended counseling to encourage smoking cessation or the use of aerosol bronchodilators or both. Participants will have pulmonary function measurements made at regular intervals for a period of 5 years. The primary outcome variable of interest is the slope of FEV_1 as a function of time.
Results to Date:
Project is in the planning phase. Clinical and statistical investigators are in the process of developing protocol, forms, and a procedures manual.
Future Plans:
Following development of protocol, training sessions will be held for clinic investigators and technicians. Patient screening, recruitment, and randomization may begin in late 1985 or early 1986.
Project Dates:
October 1984–September 1992.
Financial Support:
NHLBI (N01HR46002).

1124. UNIVERSITY OF MINNESOTA, SCHOOL OF NURSING, 6-101 Unit F, 308 Harvard Street, Minneapolis, Minnesota 55455.

Project Title:
Prevalence of Nurse Smokers and Variables Identified With Successful and Unsuccessful Smoking Cessation.

Principal Investigator:
Feldman, B.M.
Objective:
To obtain current prevalence information on registered nurses; identify variables related to smoking and smoking cessation.
Methods or Approach:
A computer-based random selection procedure was used to select 1,004 registered nurses from the State Board of Nursing files. A mailed questionnaire with two followups produced 823 completed questionnaires (82 percent response). The questionnaire was based on the literature and the researcher's own smoking experience. A pilot study utilizing the questionnaire was completed prior to distribution to subjects. Content included demographic information; checklist and open-ended items related to smoking onset; reasons, number, and results of attempts to quit; methods of quitting; reasons for successful and unsuccessful cessation attempts.
Results to Date:
Among nurses surveyed, 57.7 percent were never smokers, 18 percent were former smokers, and 24.3 percent were current smokers. The quit rate was 42.3 percent. Among those who had attempted to quit and those who had successfully quit smoking, the most frequent method used was self-directed cessation incorporating a period of tapering off and "cold turkey." "Craving to smoke" was the most frequently identified reason for recidivism. Factors identified for successful cessation were (1) a strong will to quit and never smoke another cigarette no matter what happened; and (2) pressure from spouse, family members, or significant other not to resume smoking. Information will be used to plan strategies and programs aided at reducing smoking among registered nurses and women in general.
Future Plans:
Followup of the current smoker group is continuing.
Project Dates:
October 1981–September 1985.
Financial Support:
University of Minnesota School of Nursing; ALA.

1125. UNIVERSITY OF MINNESOTA, SMOKING RESEARCH LABORATORY, Department of Psychiatry, Room 638, Diehl Hall, Minneapolis, Minnesota 55455.

Project Title:
Topographical Analysis of Smoking Behavior.

Principal Investigators:
Pickens, R.W.; Pechacek, T.F.; Hatsukami, D.K., et al.
Objective:
To perform topographical analysis of smoking behavior in a laboratory setting and in the natural environment.
Methods or Approach:
Research will (1) compare laboratory measures of ad lib smoking behavior with identical measures obtained on the same subjects in the natural environment; (2) experimentally manipulate nicotine yield of cigarettes in the laboratory and natural environment and determine effects on measures of smoking topography; (3) relate measures of smoking topography obtained with the recording device to other measures of smoking topography not obtained with the device (i.e., inhalation volume); (4) relate measures of smoking topography obtained by the device to biochemical and other measures of smoke exposure (i.e., expired air carbon monoxide, plasma cotinine, butt nicotine); (5) relate differences in cigarette smoking topography in the natural environment to the smoker's environmental situation and internal state (i.e., mood, indicated need for cigarette); (6) compare smoking topography of selected populations (men vs. women, experienced vs. inexperienced, high vs. low rate smokers) in the natural environment; and (7) determine the extent to which ad lib smoking behavior serves to maintain constant body levels of nicotine.
Results to Date:
Accuracy, reliability, and validity of the Ambulatory Smoking Recorder were tested and several modifications were made. Initial data analysis of situational factors in cigarette smoking showed significant difference in smoking topography across situations for all subjects on at least one of the topographical measures. For six of seven subjects, F values for preceding intercigarette interval were significant at $p < 0.05$, and six of seven showed significant effects of mood and need state on

smoking behavior for at least one of the dependent measures. Patterns of significant effects differed across subjects and suggest that within-subjects analysis is most appropriate for the data. Individual differences in the variables controlling smoking behavior requires further study. In preliminary data analysis, differences in puffing behavior were found in three subjects, but four showed no difference in smoking topography in the laboratory and natural environments, suggesting that the laboratory situation itself did not encourage shorter smoking episodes. Situational, mood, and need states may interact with physical environment, and data are being analyzed to control for these factors. In nine subjects examined for stability of smoke exposure across 21 consecutive days (as shown by the recording device), daily smoke exposure ranged from 38 to 516 seconds/day, reflecting large between subject differences. Smoke exposure within subjects, however, was relatively stable across days, usually within a range of 100 seconds for each subject. The smallest range of minimum to maximum smoke exposure across days was 70 seconds; the largest was 230 seconds. Data resulting from change in cigarette nicotine yield have not been analyzed.

Future Plans:
Future research will include use of a pharmacokinetic model for determining extent to which ad lib smoking behavior serves to maintain constant body levels of nicotine.

Project Dates:
July 1983–June 1986.

Financial Support:
NIDA (DA 02413).

1126. UNIVERSITY OF MINNESOTA, Department of Psychiatry, Box 393, Mayo Memorial Building, Minneapolis, Minnesota 55455.

Project Title:
Self-Administration of Nicotine Gum.

Principal Investigator:
Hughes, J.R.

Objective:
To determine patterns of self-administration of nicotine gum among smokers seen in a general medical practice who follow FDA-approved guidelines for gum use; test whether factors that control self-administration of other drugs of abuse also control self-administration of nicotine gum.

Methods or Approach:
Despite clinical evidence that both compliance with usage instructions for nicotine gum and its chronic use are substantial problems, a study of the self-administration properties of the gum has not been performed. A double-blind, placebo-controlled study will be conducted to determine the incidence of compliance and chronic use of gum and the relationship between chronic use and behavioral factors (e.g., history of abuse of other drugs). Factors that will be examined for their role in self-administration include dose (1 mg vs. 2 mg vs. 4 mg gum), response cost (free vs. half-price vs. full-price gum), schedule of self-administration (ad libitum vs. fixed times), and duration of exposure (1 vs. 2 vs. 3 months). Other studies will (1) use computerized pharmacy records to determine compliance with instructions and chronic use of gum in the first 24 months of availability; (2) use a double-blind placebo-controlled substitution study to determine whether ex-smokers develop physical dependence on the gum; (3) offer nicotine and placebo gum concurrently under different sets of instructions to determine whether self-administration is due to expectancy, placebo, or taste factors rather than pharmacologic factors; and (4) determine whether nonsmokers and ex-smokers will self-administer nicotine gum.

Results to Date:
Data indicate that self-administration of nicotine gum by abstinent smokers is not due to placebo or taste factors. However, preference for nicotine gum over placebo can be eliminated by instructions that lead subjects to believe placebo gum is as effective as nicotine gum.

Financial Support:
NIDA (1R01DA03728-01).

1127. UNIVERSITY OF MINNESOTA, DATA AND COORDINATING CENTER, Box 197 Mayo, Minneapolis, Minnesota 55414.

Project Title:
Early Intervention in Chronic Obstructive Pulmonary Disease.

Principal Investigators:
Kanner, R.E.; Buist, S.; Rogers, R.M., et al.

Objective:
To determine the effects of smoking cessation of changes in pulmonary function and symptomatology; determine effects of bronchodilator therapy on annual rate of change in forced expiratory volume in 1 sec (FEV_1) in subjects with mild airways obstruction.

Methods or Approach:
Each of 10 centers will recruit 650 subjects, cigarette smokers between 35 and 54 years of age with an FEV_1 of between 65 and 85 percent of predicted. Protocol is being developed to compare a group with no special care with a special care group that will receive an intensive smoking cessation program. In addition, bronchodilators will be given to some patients in the special care group. Over a period of at least 5 years, patients will be followed with pulmonary function studies and respiratory illness history. Comparisons will be made between the usual care and special care groups.

Results to Date:
Project is in a preliminary phase; protocol is being developed by 10 principal investigators.

Project Dates:
October 1984–March 1992.

Financial Support:
NHLBI (N01HR46014).

1128. UNIVERSITY OF MINNESOTA, 2829 University Avenue, SE., Minneapolis, Minnesota 55414.

Project Title:
Mortality Surveillance of MRFIT Screenees.

Principal Investigator:
Kjelsberg, M.O.

Objective:
To ascertain 10-year mortality among 361,622 men (aged 35 to 57) who were seen at the initial screening of the Multiple Risk Factor Intervention Trial.

Methods or Approach:
Using location of death supplied by the Social Security Administration, state departments of health will be contacted to obtain death certificates. Currently, 6-year data for all cause and cause-specific mortality are available. Definitive analyses will be performed on two major research questions: (1) association of cause-specific cancer mortality and serum cholesterol concentration; and (2) association of serum cholesterol, diastolic blood pressure, and cigarettes/day with mortality from coronary heart disease and cerebrovascular disease for black men and white men.

Results to Date:
For the association of mortality and serum cholesterol, the group represents the largest prospective cohort study yet analyzed. The additional data will allow comparisons of the association of serum cholesterol and cancer mortality to be made for different cancer sites.
Future Plans:
Future plans include development of risk prediction equations, and investigation of methodological issues associated with using Social Security Administration data files and the National Death Index.
Financial Support:
NHLBI (2R01HL28715-03).

1129. UNIVERSITY OF MINNESOTA, 2829 University Avenue, SE., Minneapolis, Minnesota 55414.

Project Title:
Multiple Risk Factor Intervention Trial.

Principal Investigator:
Kjelsberg, M.O.
Objective:
To continue as Coordinating Center for the Multiple Risk Factor Intervention Trial (MRFIT).
Methods or Approach:
The MRFIT is for primary prevention of coronary heart disease. Phase III activities, involving analysis and dissemination of data from the trial, will continue for a minimum of 3 years.
Results to Date:
Results are not available.
Financial Support:
NHLBI, Division of Heart and Vascular Diseases (5N01HV22971-18).

1130. UNIVERSITY OF MINNESOTA, 2829 University Avenue, SE., Minneapolis, Minnesota 55414.

Project Title:
Diet, Vitamin A, Serum Retinol, Beta-Carotene and Cancer in MRFIT.

Principal Investigator:
Kjelsberg, M.O.
Objective:
To study the relationship between cancer mortality and dietary vitamin A and beta-carotene, and serum retinol and beta-carotene.
Methods or Approach:
Data collected as part of the Multiple Risk Factor Intervention Trial (MRFIT) were used. Multiple 24-hour dietary recalls collected annually on 12,866 men over an average followup period of 7 years will be used for dietary analysis. Mortality followup is proposed through June 1986, which will result in an average followup period of 11 years and an estimated 300 cancer deaths, with an estimated 100 to 125 lung cancer deaths. Data will permit associations to be studied, controlling for initial smoking and lipid levels, changes in smoking and plasma lipoproteins, socioeconomic status, alcohol intake, and occupation.
Results to Date:
Project is in a preliminary phase.
Financial Support:
NCI (5R01CA34263-02).

1131. UNIVERSITY OF MINNESOTA, Division of Epidemiology, 611 Beacon Street, SE., Stadium Gate 27, Minneapolis, Minnesota 55455.

Project Title:
Developmental Approach to Adolescent Smoking Prevention.

Principal Investigators:
Murray, D.M.; Perry, C.L.
Objective:
To monitor cigarette smoking habits of two consecutive cohorts of adolescents as they move through high school to determine whether a 7th grade smoking prevention program will be effective in significantly reducing smoking prevalence and incidence rates through the 12th grade.
Methods or Approach:
Sixty percent of the students were exposed to the experimental smoking prevention program in seventh grade. Half of the members in each cohort, selected randomly, will be exposed to a new 10th grade treatment program. It is suspected that the initial effect of the seventh grade program will diminish as students move into high school and that an effective 10th grade program will be necessary to maintain the initial reduction in smoking. The crossed study design will permit examination of the 7th and 10th grade programs alone and in combination. The 10th grade program addresses the functions served by drug use in this age group and promotes healthy alternatives to drug use. The model considers environmental and personal or idiosyncratic influence systems that interact to shape adolescent health behavior. While testing the efficacy of the programs, the adequacy of the model in accounting for smoking changes in the cohorts and for the effects attributable to the treatments will be evaluated.
Results to Date:
Results are not yet available.
Project Dates:
September 1982–August 1985.
Financial Support:
NIDA (R01DA/HD03205).

1132. UNIVERSITY OF MINNESOTA, Division of Epidemiology, 611 Beacon Street, SE., Stadium Gate 27, Minneapolis, Minnesota 55455.

Project Title:
Tailoring Drug Abuse Prevention to the School Setting.

Principal Investigators:
Murray, D.M.; Perry, C.L.
Objective:
To evaluate classroom-based drug abuse prevention programs in isolation and in combination with efforts to modify the adolescent's environment related to drug use.
Methods or Approach:
Twelve schools were randomized to one of the following conditions: (1) classroom prevention program based on peer leadership, teaching pressure-resisting skills, and promoting healthy alternatives to drug use; (2) the same program combined with schoolwide and parent activities designed to promote nonuse in the broader environment; or (3) control condition. Evaluation is based on chemically validated self-reports taken at baseline and at 3-month and 15-month followup.
Results to Date:
All interventions were complete and 3-month followup data had been collected by February 1985. Analysis has not been completed.

Project Dates:
June 1983–May 1986.
Financial Support:
NIDA (R01DA03044).

1133. UNIVERSITY OF MINNESOTA, Division of Epidemiology, 611 Beacon Street, SE., Stadium Gate 27, Minneapolis, Minnesota 55455.

Project Title:
Evaluation of School Based Smoking Prevention.

Principal Investigators:
Murray, D.M.; Luepker, R.V.; Pirie, P., et al.
Objective:
To evaluate the long-term effects of a seventh grade smoking prevention program.
Methods or Approach:
Long-term followup of school-based smoking prevention programs that appear successful is essential; short-term effects may fade over time and it is even possible that programs that initially appear to be ineffective may prove valuable in the long term. At minimum, it is important to determine whether the short-term effects are maintained into adulthood. The period from high school to the mid-twenties is important because there is relatively little longitudinal data available on smoking during this period of rapid social development. The study will follow 7,000 students who participated in seventh grade prevention programs through the age of 25. Three cohorts have participated in three earlier studies since 1979; 70 percent are still in their original school districts and are still subjects of ongoing study. The project will try to locate the 30 percent who have left their original schools to obtain locator data to permit annual tracking through 1993. Telephone and personal interviews will be used to monitor smoking and environmental and psychosocial variables related to smoking. The new data will be linked to the existing 4-year data base for longitudinal evaluation of the earlier prevention programs. In addition, data will provide important new information on factors that influence smoking from high school graduation through young adulthood.
Results to Date:
Project is in a preliminary phase.
Future Plans:
July 1984–June 1989.
Financial Support:
NCI (R01CA38275).

1134. UNIVERSITY OF MINNESOTA, 299 McNeal Hall, 1985 Buford Avenue, St. Paul, Minnesota 55108.

Project Title:
Family Functioning and Adolescent Substance Use.

Principal Investigators:
Needle, R.H.; McCubbin, H.
Objective:
To study adolescent use of cigarettes, alcohol, marijuana, and other drugs in relation to (1) family functioning (adaptability, cohesion, communication, family stressors and strains, family coping), (2) adolescent role strains that emerge from roles as sons or daughters, siblings, friends, and students; (3) coping behaviors and personal resources (mastery and self-esteem) in managing problems of difficult situations that happen to them or members of the family, and (4) substance use patterns and perceived attitudes toward drug use of parents, older siblings, and peers.
Methods or Approach:
Survey interview methodology was employed to obtain data on variables of family system functioning; family stressors and strains; adolescent stress, strain, and coping; and substance use from focal adolescents (aged 11, 12, and 13 in 1981), older siblings, and parents. Interviews were conducted in the home. The two major dependent variables were (1) stage of drug use and (2) frequency of use of different substances. Families were drawn from a large health maintenance organization; 508 of the families (43 percent) who had at least one adolescent aged 11, 12, or 13 (n = 525) agreed to participate. After 3 years, 498 families were still participating. Examination of institutional records of the health maintenance organization showed no significant differences between participating families and nonparticipating families in use of chemical dependency services.
Results to Date:
In 1982 (first year of data collection), 28 percent of focal adolescents reported ever using cigarettes. In 1984, the proportion increased to 49 percent. For older siblings of focal subjects, rates of use were greater. Focal adolescents who used cigarettes were more likely to use marijuana than those who did not report using cigarettes. Parental, older sibling, and peer attitudes toward substance use, as perceived by study subjects, were related to substance use, including cigarettes. For all substances, peer drug-using behavior (as perceived by the adolescent) correlates most strongly with adolescent use of different drugs. For each substance, focal adolescents were more likely to report using, and using frequently, if older siblings were using the substance and using it frequently. (Data are based on independent information provided by older siblings and focal adolescents.) For cigarettes and other substances, peer substance use and sibling substance use had unique effects on use by focal adolescents.
Future Plans:
A proposed 3-year continuation would build on the foundation of baseline data obtained to advance knowledge of critical family predictors of stages of adolescent substance use. Observation methods to further examine family interactions are included.
Project Dates:
April 1980–September 1935.
Financial Support:
NIDA (R01DA02560).

1135. UNIVERSITY OF MINNESOTA, SCHOOL OF PUBLIC HEALTH, Division of Epidemiology, Stadium Gate 27, 611 Beacon Street, SE., Minneapolis, Minnesota 55455.

Project Title:
Community-Based Smoking Prevention: Youth Education and the Minnesota Heart Health Program.

Principal Investigators:
Perry, C.L.; Halper, A.; Klepp, K.-I., et al.
Objective:
To enhance cardiovascular health and reduce morbidity and mortality from cardiovascular diseases in three north-central communities in Minnesota.
Methods or Approach:
The Minnesota Heart Health Program is a community-based demonstration project involving a 9-year education program in the communities, annual risk factor assessments on a sample of adult populations in the three "educated" communities and three comparison communities, and morbidity and mortality surveillance. Targeted objectives of the education program, aimed at the entire community, include significant changes in

smoking prevalence, eating patterns, physical activity, and hypertension management. Youth are viewed as a specific target group within the larger education program; smoking is a targeted behavior. Antismoking interventions for youth are part of a larger effort to promote health in this age group. Smoking prevention efforts utilize three general types of intervention strategies: communitywide antismoking campaigns, peer-led educational interventions with seventh and ninth grade students, and community organization activities to modify social and environmental factors. Ongoing research to test efficacy of programs involves outcome analyses of individual educational interventions, effects of programs on parental smoking behavior, and a longitudinal study (1983-1989) of the Class of 1989 in one educated and one comparison community to assess effects of all strategies on health behavior development during adolescence.

Results to Date:
Short-term results of the seventh grade smoking prevention program demonstrate significant reductions in onset rates in treatment schools. Parents of students in the high school intervention program had more awareness of smoking prevention and more conversations with their children. Parents were three times as likely to quit smoking during the antismoking campaign as people without children. Results of the longitudinal study are not yet available.

Future Plans:
The longitudinal study will be continued, with followup interventions in 1985-1986 and 1986-1987. Expansion of the smoking prevention focus will include other health-compromising behaviors.

Project Dates:
July 1980–June 1990.

Financial Support:
NHLBI (1R01HL25523).

1136. UNIVERSITY OF MINNESOTA, Department of Psychiatry, Box 393, Mayo Memorial Building, Minneapolis, Minnesota 55455.

Project Title:
Smoking as a Dependence Process.

Principal Investigator:
Hughes, J.R.

Objective:
To investigate smoking as a dependence process.

Methods or Approach:
Two research designs will be used. The first study will investigate undeprived smokers, deprived smokers and nonsmokers to determine whether smoking cessation impairs response inhibition on a psychomotor task. The second study will use a population-based random sample of smokers in Minneapolis-Saint Paul to determine current and lifetime prevalence of tobacco dependence and withdrawal according to current standards such as DSM-III and Fagerstrom's Tolerance Scale.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Following the second study, tests will be done to determine whether nicotine will reverse any cessation-induced decrements in response inhibition.

Project Dates:
April 1985–March 1990.

Financial Support:
University of Minnesota; NIDA.

1137. UNIVERSITY OF MINNESOTA, MINNEAPOLIS, Department of Medicine, Cardiovascular Division, Box 508, Mayo, 420 Delaware Street, S.E., Minneapolis, Minnesota 55455.

Project Title:
Doctors Helping Smokers - A Clinical Trial.

Principal Investigator:
Kottke, T.E.

Objective:
To (1) develop and test a program that will teach physicians to integrate smoking cessation activities into practice routines; (2) identify factors impeding delivery of the nonsmoking message in private practices; (3) determine if special training workshops can increase smoking cessation rates among patients seen by those physicians; and (4) increase physician participation in the smoking cessation effort.

Methods or Approach:
Physicians will be randomly allocated to one of three groups: (1) control, which will be asked to conduct a month-long smoking cessation campaign without further assistance; (2) special materials group, which will be given unlimited access to a self-help smoking cessation program of proven effectiveness and written instructions for using nicotine gum; and (3) trained group, which will receive a 1-day training workshop, unlimited access to a self-help smoking cessation program, and instructions for using nicotine chewing gum. Physicians in each group will be asked to identify all smokers during a month-long campaign and try to obtain a commitment from them to stop smoking. Randomly selected patients will be telephoned for a short interview to determine smoking cessation and success rates. They will be called three times in a 2-year period.

Results to Date:
Project is in a preliminary phase.

Project Dates:
July 1984–July 1989.

Financial Support:
NCI (1R01CA38361-01).

1138. VETERANS ADMINISTRATION MEDICAL CENTER, 4801 54th Street E., Minneapolis, Minnesota 55417.

Project Title:
Measurement of the Transmucosal Potential Difference in the Intact Airway.

Principal Investigator:
Hale, K.A.

Objective:
To investigate the relative importance of different pathophysiologic factors that may cause alveolar hypoxia, including structural changes such as airways disease, emphysema, and disorders of ventilatory control.

Methods or Approach:
Patients scheduled to undergo thoracotomy for coin lesions were studied. Preoperative assessments were made of pulmonary function, ventilatory response to hypercarbia, and eucapnic hypoxia and ventilatory disturbances during sleep. Tissue resected at thoracotomy was evaluated pathologically for the presence of emphysema, airways disease, and vascular disease. Using the muscular pulmonary artery morphology as an index of pulmonary vascular disease, the pulmonary artery morphologic change was correlated with the structural changes as measured by the degree of airways disease and emphysema and the control of ventilation as measured by sleep studies and responses to hypercarbia and hypoxia.

Results to Date:
To date, 11 patients have been studied preoperatively. In three, inadequate tissue was resected or metastatic disease was present and no resection was done. Eight lungs were available for examination and correlation with morphology. The vascular changes in these lungs were relatively mild when compared with lungs of other cigarette smokers. There were few abnormalities of respiratory control during sleep or while awake and the structural changes were minimal, especially the lack of emphysema. Airways disease appears to correlate best with the minimal pulmonary vascular changes.
Financial Support:
VA.

Mississippi

1139. VETERANS ADMINISTRATION MEDICAL CENTER, 1500 East Woodrow Wilson Drive, Jackson, Mississippi 39216.

Project Title:
Comprehensive Evaluation of Smoking Risk Reduction Procedures.

Principal Investigators:
Martin, J.E.; Prue, D.M.
Objective:
To comprehensively evaluate long-term efficacy of a gradual reduction procedure to low tar and nicotine cigarettes on smokers; determine reactive effects and reliability of various methods of assessing smoking exposure.
Methods or Approach:
Study 1 will evaluate long-term effectiveness of a progressive brand-change approach to smoking treatment and risk reduction. Smokers will receive brand-fading with and without behavioral abstinence training. In addition, effects of a smoking exposure feedback condition (e.g., carbon monoxide, CO), thiocyanate (SCN) will be compared with a no-feedback condition within each group. Study 2 will assess effects of progressively more intensive self-monitoring procedures on treatment dropouts. Study 1 subjects will self-monitor smoking rate; alveolar CO and saliva SCN measurements will be made at weekly sessions across baseline, brand-fading, and followup phases. Subjects will be assigned to two variations of brand-fading. Study 2 subjects will be assigned to various home self-monitoring procedures before and during brand-fading treatment. Attendance/dropout rates will be compared for each group. Changes in smoking-related cardiovascular risk will be evaluated. Differences in risk reduction are expected between the two brand-fading conditions.
Results to Date:
Results are not yet available.
Financial Support:
VA.

Missouri

1140. JEWISH HOSPITAL OF ST. LOUIS, 216 South Kingshighway, St. Louis, Missouri 63110.

Project Title:
Modulation of Extracellular Neutrophil Elastase Activity.

Principal Investigator:
Campbell, E.J.
Objective:
To (1) study the in vitro binding and internalization of neutrophil elastase by alveolar macrophages with regard to the nature of the macrophage receptor for elastase, the enzymatic activity of internalized enzyme, the intracellular localization of internalized enzyme relative to the macrophage inhibitor of elastase, and conditions that promote release of elastase previously internalized by macrophages; (2) quantify the fraction of oxidized α_1-proteinase inhibitor in plasma and bronchoalveolar lavage fluid from human nonsmokers and cigarette smokers; and (3) relate results to smoking history, respiratory symptoms, and degree of ventilatory impairment.
Methods or Approach:
Elastase released from neutrophils during inflammation has been implicated in the pathogenesis of tissue injury in a number of disease processes including pulmonary emphysema. Control of extracellular neutrophil elastase activity depends on proteinase inhibitors (primarily α_1-proteinase inhibitor and α_2-macroglobulin) and on interaction with the mononuclear phagocyte system. Because α_2-macroglobulin is absent (or present in low concentrations) in the lower respiratory tract and interstitial space, control of released elastase in these locations would be expected to depend on inhibition by α_1-proteinase inhibitor and binding of active enzyme to alveolar (and interstitial) macrophages. It is hypothesized that inactivation of α_1-proteinase inhibitor by oxidants (including oxidants from cigarette smoke and activated neutrophils) increases risk of tissue injury during inflammation, and also causes the mononuclear phagocyte system to assume greater importance in antielastase defenses. It is anticipated that the improved insight into control of released neutrophil elastase activity in health and disease will be helpful in developing strategies for limitation of proteolytic tissue injury in diseases such as pulmonary emphysema.
Results to Date:
Project is in a preliminary phase.
Financial Support:
NHLBI (5R01HL30341-02).

1141. KANSAS CITY, MISSOURI HEALTH DEPARTMENT, Office of Health Research and Analysis, Kansas City, Missouri 64106.

Project Title:
Infant Mortality 1983: An Update. Low Birth Weight Costs and Prevention.

Principal Investigator:
Welch, Q.B.

Objective:
To (1) determine infant mortality rate by race in Kansas City in 1983; (2) compare rates with those of the State, the United States, and various countries around the world for 1979 and 1982; (3) analyze relationship of prenatal care, smoking, race, marital status, age, education, and residency to low birth weight; and (4) determine the reduction in costs achievable by reducing risk factors.

Methods or Approach:
Log-linear statistical methodology was used to analyze birth weights of over 62,000 infants born to Kansas City residents and to nonresidents (who delivered within the city limits) with respect to variables associated with low birth weight.

Results to Date:
Inadequate prenatal care, smoking, and being nonwhite were statistically significant risk factors for low birth weight; only 7.1 percent of black women with no risk factors had low birth weight infants compared with 15.2 percent of black women who smoked. The impact of smoking approximately doubles the risk of low birth weight in both whites and nonwhites, and lack of prenatal care for mothers who smoked was an additive risk; the number of low birth weight infants among black mothers who smoked increased to 21.4 percent among those with inadequate prenatal care (for white mothers, combined risk was 20.8 percent). Total costs for both infant care and a smoking cessation program are less than costs without any intervention. Compared with nonresidents, Kansas City residents tend to be younger and less educated, fewer are married, and more are smokers; 33.2 percent of residents were smokers in 1983 (34.9 percent in 1979) compared with 28.8 percent of nonresidents (30.4 percent in 1979).

Financial Support:
Kansas City, Missouri, Health Department.

Reference:
Welch, Q.B. *Infant Mortality 1983: An Update. Low Birth Weight Costs and Prevention.* Kansas City, Missouri Health Department, Office of Health Research and Analysis, October 5, 1984, 27 pp.

1142. MIDWEST RESEARCH INSTITUTE, 425 Volker Boulevard, Kansas City, Missouri 64110.

Project Title:
Identification of Variables Associated With the Maintenance of Nonsmoking in Ex-Smokers.

Principal Investigator:
O'Connell, K.A.

Objective:
To determine what factors may be associated with long-term maintenance of abstinence and with recidivism among former cigarette smokers.

Methods or Approach:
Persons participating in community-based smoking-cessation programs are followed up over time. All persons are screened at the beginning of their cessation programs with a comprehensive questionnaire. A telephone followup 3 months after completion of the program is conducted to determine smoking status. Abstinent individuals then are followed up in person at 3, 6, and 12 months following completion of their respective programs. A variety of situational, attitudinal, and health variables are assessed through interviews and questionnaires. Particular attention is devoted to factors that are potentially modifiable by cessation programs. Abstinence from smoking is validated by assessment of salivary thiocyanate levels.

Results to Date:
Multivariate analyses supported the interpretation that predictors of short-term cessation were different from, and often the reverse of, predictors of long-term cessation. Results indicate that subjects who need to quit smoking the most (those with abnormal pulmonary function tests or who have been advised to quit for health reasons) are often the subjects who have the least success. Also, subjects who have the least trouble with the early phases of cessation may be the ones who are the most vulnerable to late relapse. The finding relating late relapse with stressful life events emphasizes the role of smoking as a coping strategy and points to the need to train smokers to use coping strategies other than smoking to deal with stress.

Project Dates:
September 1980–1984.

Financial Support:
NHLBI (NO1-HR-0-2917).

1143. UNIVERSITY OF MISSOURI, HEALTH SCIENCE CENTER, M470, Columbia, Missouri 65121.

Project Title:
As Assessment of the Practice of Preventive Cardiology in an Academic Health Center.

Principal Investigators:
Otradovec, K.; Blake, R.L., Jr.; Parker, B.M.

Objective:
To determine how often the risk factors of cardiovascular disease are assessed and appropriate modification suggested in new clinic patients seen in three primary care departments (medicine, family medicine, and pediatrics).

Methods or Approach:
Random selection of outpatient charts was carried out in the three departments, and information pertaining to cardiovascular risk factors was collected using a chart audit form. Cigarette smoking was one of the risk factors assessed. All patient visits were scrutinized for evidence of risk factor assessment.

Results to Date:
Risk factors for cardiovascular disease were assessed infrequently, and there was little evidence that modification was attempted when risks were identified. Data from outpatient charts indicate that smoking was queried in only 34 percent (medicine), 24 percent (family medicine), and 6 percent (pediatrics) of visits.

Project Dates:
June 1982–March 1986.

Financial Support:
University of Missouri, Department of Medicine; NHLBI (HL 00979).

1144. UNIVERSITY OF MISSOURI, COLUMBIA, Department of Chemistry, 123 Chemistry Building, Columbia, Missouri 65221.

Project Title:
Carcinogenesis: Nitrosamine Formation and Inhibition.

Principal Investigator:
Loeppky, R.N.

Objective:
To (1) determine how nitrosamines form in the environment; (2) study tertiary amines and other ternary nitrogen compounds that might give rise to nitrosamines; (3) elucidate the chemical processes that produce nitrosamines from these compounds; and (4) develop methods for inhibition of nitrosamine formation when the mechanism of nitrosamine production is revealed.

Methods or Approach:
Methods are those of studying reaction mechanisms of organic chemistry; structures are varied to determine reactivity of substances. Reaction kinetics are used to elucidate the paths by which nitrosamines are forming. Various compounds are employed to determine whether they can block nitrosamine formation.

Results to Date:
A group of tertiary amines that react with acidic nitrite to produce nitrosamines almost instantaneously has been identified, and it has been shown that electron-rich aromatic compounds bonded through a CH_2 group (or other carbon fragment) to a dialkylated nitrogen atom rapidly react with nitrous acid to produce nitrosamines. Certain molecules that are effective at blocking the process and a new type of nitrosation process that involves ionic nitrite have also been discovered. When amines are heated with ionic nitrite in the presence of nonvolatile esters, relatively rapid nitrosation takes place. The chemical steps in this process have been investigated, and the reaction scheme suggests that the formation of nitrosamines in products that are formulated to contain amines may be preventable.

Project Dates:
April 1984–April 1986.

Financial Support:
NCI (CA 26914).

1145. UNIVERSITY OF MISSOURI, COLUMBIA, Department of Chemistry, 123 Chemistry Building, Columbia, Missouri 65211.

Project Title:
Nitrosamine Fragmentation and Nitrosamine Carcinogenesis.

Principal Investigator:
Loeppky, R.N.

Objective:
To investigate the chemical and biochemical processes that are responsible for chain-shortening reactions of β-oxidized nitrosamines; determine whether there is a biochemical pathway analagous to the retro aldol fragmentation reaction of β-hydroxy and β-keto nitrosamines.

Methods or Approach:
Research will synthesize model β-hydroxy and β-keto nitrosamines or use ones that are found in the environment to investigate whether specific fractions of rat liver or other animal tissue are capable of producing chain-shortening reactions.

Results to Date:
Data indicate that there is a biochemical transformation that causes cleavage of β-hydroxy nitrosamines and generates methylalkyl nitrosamines in their place. The methylalkyl nitrosamines can then be degraded further by other metabolic processes to lead to methylation of important biomolecules.

Future Plans:
Research will determine reliable conditions for observing the biochemical fragmentation of β-hydroxy nitrosamines and investigate the scope of this process by determining what enzymes may be responsible for this degradation.

Project Dates:
May 1984–May 1986.

Financial Support:
NCI (CA 22289).

1146. VETERANS ADMINISTRATION MEDICAL CENTER, 4801 Linwood Boulevard, Kansas City, Missouri 64128.

Project Title:
Venoruton and Smoking-Induced Changes in Endothelial Cells.

Principal Investigators:
Davis, J.W.; Hartman, C.R.

Objective:
To compare the effects of a mixture of hydroxyethylrutosides (Venoruton) and a placebo on the following responses to cigarette smoking: (1) increase in circulating endothelial cells; (2) decrease in platelet aggregate ratio; and (3) increase in platelet factor 4 and B-thromboglobulin in platelet-poor plasma.

Methods or Approach:
A random-order, double-blind, crossover design was used to compare hydroxyethylrutosides with placebo in healthy volunteers of both sexes. Circulating endothelial cells, platelet aggregate ratio, and platelet factor 4 were determined immediately before and after each of two 20-minute periods during which two cigarettes were smoked. The two smoking periods were separated by at least 2 weeks and preceded by four doses of medication or placebo during the 24 hours before smoking. Differential centrifugation and phase-contrast microscopy were used in determination of circulating endothelial cells and platelet aggregate ratio. Platelet factor 4 and B-thromboglobulin were determined by radioimmunoassay.

Results to Date:
After smoking, there was a statistically significant increase in mean value of endothelial cell count and concentration of β-thromboglobulin and a significant decrease in mean platelet aggregate ratio, whether or not Venoruton or placebo had been taken. Smoking-induced changes after Venoruton were not significantly different from changes after placebo for any variable.

Project Dates:
1981–1983.

1147. VETERANS ADMINISTRATION MEDICAL CENTER, 915 North Grand Boulevard, St. Louis, Missouri 63106.

Project Title.
Elastase Secretion by Alveolar Macrophages–Response to Various Agents and Difference Between Species.

Principal Investigator:
Levine, E.A.

Objective:
To develop a desmosine immunoassay capable of detecting as little as 0.3 picomoles of desmosine in urinary samples to detect in vivo elastin degradation.

Methods or Approach:
The immunoassay has been used to measure elastin degradation in patients with chronic obstructive lung disease or acute lung infection or in patients who are heavy smokers. Animal models have been used for controlled conditions.

Results to Date:
Most patients tested were shown to excrete a higher amount of desmosine. Twenty-four hours after instillation of four different groups of rats, via the trachea, with 0, 5, 10, and 20 m units of pancreatic elastase, the immunoassay detected 0.17, 0.92, 0.88, and 3.27 nmol desmosine, respectively. Results showed that desmosine excretion increased in response to increased doses of elastase. It is concluded that the immunoassay may be

a sensitive indicator of pulmonary elastolysis that would not be detectable using conventional methods, and that the immunoassay technique is probably useful for diagnosis of human disease.

Financial Support:
VA.

1148. VETERANS ADMINISTRATION MEDICAL CENTER, 915 North Grand Boulevard, St. Louis, Missouri 63106.

Project Title:
Studies of Protease Inhibitors.

Principal Investigator:
Pierce, J.A.

Objective:
To reexamine the functional status of α_1-proteinase inhibitor (α_1Pi) in bronchoalveolar lavage (BAL) fluid obtained from healthy nonsmoking subjects, healthy cigarette smokers, patients with obstructive airways disease, and subjects with the classic deficiency of α_1Pi; understand more about the biology of reactions between α_1Pi and the cells that may be involved in remodeling the architecture of the lung.

Methods or Approach:
Oxidation of α_1Pi as produced by cells contained in BAL fluid will be measured and the type and number of cells will be correlated with the quantity of oxidated α_1Pi. Finally, oxidized hamster α_1Pi will be studied in vivo to determine its persistence in blood and in the lung. The experiments are important to further understanding of the pathogenesis of emphysema, especially to better define the role of oxidative reaction on occurrence of extracellular elastolysis.

Results to Date:
Project is in a preliminary phase.

Financial Support:
VA.

1149. VETERANS ADMINISTRATION, 4801 Linwood Boulevard, Kansas City, Missouri 64128.

Project Title:
Multiple Stage Treatment Program for Smoking Reduction.

Principal Investigators:
Keyser, D.J.; Palmer, R.D.

Objective:
To test a novel method of smoking reduction on a diverse population; refine and attempt to automate this smoking reduction therapy so that it can be offered to Veterans Administration patients and employees on a continuous basis through the psychology service.

Methods or Approach:
The proposed treatment entails a three-stage process designed to (1) induce commitment to treatment and create an expectation of change; (2) offer smokers a response (i.e., relaxation) with which to combat the temporary discomfort associated with resisting cigarettes; and (3) creating a state of social dissonance with regard to smoking (i.e., demonstrating to smokers how their behavior negatively influences others). The proposed treatment will be implemented over a 3-week period via direct verbal and tape-recorded interventions. The treatment will be contrasted with a nonspecific factors control group and an untreated control. The data will be analyzed via a 2 (treatments) x 5 (periods: 3 treatment weeks and a 1 and 4 month followup) ANOVA design with repeated measures on one factor. Percent of baseline smoking will be employed as the dependent variable.

Results to Date:
Project is in a preliminary phase.

Financial Support:
VA.

1150. WASHINGTON UNIVERSITY, Department of Psychology, Campus Box 1125, St. Louis, Missouri 63130.

Project Title:
EASE (Employer Assisted Smoking Elimination).

Principal Investigators:
Fisher, E.B., Jr.; Bishop, D.B.

Objective:
To develop multicomponent smoking cessation programs in the workplace that would harness social and institutional forces that would encourage both quitting and long-term abstinence.

Methods or Approach:
It was hypothesized that both smoking and nonsmoking employees would share knowledge and concern about smoking, thereby raising awareness and interest of coworkers. It was expected that employees would recruit others into programs and provide support for quitting and maintenance. Coworker support is encouraged by involving employees in program staging and management. An ongoing series of activities was planned for each worksite rather than a single clinic; employers and personnel were guided in tailoring program procedures to the characteristics of individual worksites and in developing an ongoing program to encourage maintenance of cessation. A steering committee at each worksite (representatives from management and line employees) tailors the basic EASE program to fit the needs of the particular worksite. At an organizational meeting, interested employees select from among three cessation procedures: (1) self-help, (2) self-help plus troubleshooting, and (3) group comprehensive clinic. In self-help, participants are given Freedom From Smoking self-help manuals developed by the American Lung Association; in the troubleshooting option, participants are given the manuals and are expected to attend four group meetings over a 6-week period. The group comprehensive clinic (nine meetings scheduled over a 7-week period) is based on the Freedom From Smoking Clinic developed by the American Lung Association, but modified for the workplace (meetings tailored to standard lunch hours).

Results to Date:
EASE was initiated in nine worksites over a period of 2 years; in four sites, the three-track program has been offered twice or more. At each company, employees have been trained to run the clinics. Workforces range from 200 to 6,000 employees, providing broad and representative settings in which to evaluate program effectiveness. At the first two sites, 12-month followup data is available. At one company with 190 employees, 18 of 63 smokers became actively involved in the program and 6 were abstinent 12 months after quitting. EASE was the probable impetus for four other employees who quit without joining the program; thus, the direct and indirect effects included 15.8 percent of all smoking employees being abstinent at 12-month followup. At the second site (180 employees, 62 smokers), all smokers received self-help manuals and 38 percent participated actively in the clinics. Overall abstinence at 12-month followup was 26 percent, increasing to 33 percent when only those still with the company are included.

Future Plans:
When data analysis is complete, results will be published, focusing on the impact of the social fabric of the workplace in maintaining abstinence following cessation. It is anticipated

that major portions of the program as it has been developed will be made available through the American Lung Association to worksites nationally and in the St. Louis area.

Project Dates:
September 1982–August 1985.

Financial Support:
ALA.

1151. WASHINGTON UNIVERSITY, Barnes Hospital Plaza, Suite 16413, St. Louis, Missouri 63110-1318.

Project Title:
Collaborative Study to Determine Risk of Lung Disease.

Principal Investigators:
Bruce, R.M.; Cohen, B.H.; Diamond, E.H., et al.

Objective:
To assess risk of lung disease in random populations using multivariate analysis, controlling for age, sex, cigarette smoking history, race, and α_1-antitrypsin phenotype, by study center and socioeconomic status.

Methods or Approach:
The 143 Pi MZ heterozygous (MZ) subjects identified from random populations were closely matched with Pi M controls from the same population at six study centers. An expanded National Heart, Lung and Blood Institute respiratory symptom questionnaire was completed by each subject. Pulmonary function tests, designed to detect established as well as early obstructive airway abnormalities, were administered.

Results to Date:
Multivariate analysis of the variance of data from the questionnaire and pulmonary function tests, corrected for age, race, sex, and smoking history, showed no significant difference between subjects of Pi MZ and Pi M phenotype. However, results confirm that smoking and advancing age adversely affect lung function. It is concluded that MZ phenotype alone carries no greater risk of developing lung disease than M phenotype.

Financial Support:
NHLBI (HR-72909; HR-72910; HR-72912; HR-72907; HR-72913; HR-72908).

Reference:
Bruce, R.M.; Cohen, B.H.; Diamond, E.L., et al. "Collaborative Study to Assess Risk of Lung Disease in Pi MZ Phenotype Subjects." *American Review of Respiratory Diseases* 130:386-390, 1984.

Nebraska

1152. CREIGHTON UNIVERSITY, SCHOOL OF MEDICINE, 601 North 30th Street, Omaha, Nebraska 68131.

Project Title:
Carboxyhemoglobin Levels in Banked Blood.

Principal Investigators:
Aronow, W.S.; O'Donohue, W.J., Jr.

Objective:
To investigate the prevalence of carboxyhemoglobin levels in banked blood at St. Joseph Hospital (Creighton University) that exceeded air quality standards (1.5 percent).

Methods or Approach:
Exposure to carbon monoxide from smoking or heavy atmospheric carbon monoxide pollution impairs cardiovascular function in patients with cardiovascular or chronic obstructive pulmonary disease. There is a potential risk for patients when transfused with blood containing high levels of carboxyhemoglobin. Banked blood from 101 randomly selected samples provided by the hospital blood bank was analyzed for carboxyhemoglobin between October 1982 and March 1983. Two tubing segments per unit of stored blood were placed in 10 mL tubes with chilled water and rotated on a hematologic mixer for 6 hours. Data were recorded and averaged.

Results to Date:
Of 101 units of blood, 49 had carboxyhemoglobin levels greater than 1.5 percent and 36 had levels of 2.0 or more. The highest level observed was 12.0 percent. It may be undesirable to use blood with increased carboxyhemoglobin content when multiple transfusions are necessary; labeling would help avoid consecutive transfusions of blood with high carboxyhemoglobin levels.

Project Dates:
October 1982–March 1983.

Financial Support:
Creighton University School of Medicine.

Reference:
Aronow, W.S.; O'Donohue, W.J., Jr.; Freygang, J., et al. "Carboxyhemoglobin Levels in Banked Blood." *Chest* 85:694-695, May 1984.

1153. CREIGHTON UNIVERSITY, ALLERGIC DISEASE CENTER, 2500 California Street, Omaha, Nebraska 68178.

Project Title:
In Vitro Effects of Cigarette Smoking and Nicotine on Leukotriene D_4 Receptors in Peripheral Lung and Alveolar Macrophages.

Principal Investigators:
Townley, R.G.; Takeyama, H.F.

Objective:
To test the null hypothesis that nicotine regulates leukotriene D_4-induced responses in airway smooth muscle and alveolar macrophages by interacting directly with a leukotriene D_4 receptor system.

Methods or Approach:
The established leukotriene receptor binding assay will be used. Direct in vitro effects of nicotine and cigarette smoking on activity (affinity, concentration, regulation) and function of leukotriene D_4 receptor binding sites will be quantified. Determination will be made of in vitro effects of smoking and nicotine on activity of receptors in airways and alveolar macrophages from guinea pigs. Changes in airway receptor activity will be correlated with results of effects on muscle functional response. Smoking and nicotine effects on function and activity of leukotriene D_4 receptor will be also be compared with effects on a β-adrenergic receptor system in the same tissue or cells.

Results to Date:
Using ^{3}H-leukotriene D_4, the leukotriene D_4 receptor system in peripheral airways and alveolar macrophages was characterized and binding results with leukotriene-induced contractile

responses were correlated. In vitro effects of guanine-5-triphosphate and Mg^{2+} on leukotriene D_4 binding was assessed. Chronic antigen- (egg albumin) or histamine-induced bronchospasm significantly increased number of leukotriene D_4 receptors. Chronic corticosteroid administration significantly increased number of leukotriene D_4 and B_4 receptors in guinea pig lung. Incubation of guinea pig lung with 10^{-3}M nicotine caused a 26 percent decrease in number of β-adrenergic receptors.

Future Plans:

Smoking and nicotine will be examined for direct effects on in vitro release of leukotrienes from macrophages. Results will be used to support or reject the null hypothesis.

Project Dates:

June 1984–May 1986.

Financial Support:

Nebraska State Department of Health, Smoking Disease and Cancer Program (85-07).

1154. UNIVERSITY OF NEBRASKA MEDICAL CENTER, EPPLEY INSTITUTE FOR RESEARCH IN CANCER AND ALLIED DISEASES, 42nd and Dewey Avenue, Omaha, Nebraska 68105.

Project Title:

Laboratory Cancer Research Center Support (CORE) Grant.

Principal Investigator:

Bresnick, E.

Objective:

To establish a Laboratory Cancer Research Center (CORE).

Methods or Approach:

Goals are being met by a team of pathologists, virologists, biologists, nutritionists, pharmacologists, chemists, biochemists, and cell/molecular biologists working in a collaborative manner in establishment of CORE-supported research facilities and research groups; sponsorship of cancer-related symposia for professionals and laymen; submission of an expansion grant request to further cancer research; publication of "Update," a cancer research newsletter; and development of a cancer data base in conjunction with the University of Nebraska Medical Center.

Results to Date:

The center will (1) foster research in chemical carcinogenesis, particularly as it relates to nitrogen-containing organic compounds, certain chemotherapeutic agents, and polycyclic aromatic hydrocarbons; (2) develop model systems for the study of the counterparts to human colon, pancreas, esophagus, prostate, and lung cancer; (3) develop an understanding of the mechanisms of activation of procarcinogens and of detoxification of carcinogens and elucidate the contributions of nutrition, environment, and genetics to their regulation; (4) clarify the role of DNA repair in mutagenesis and carcinogenesis; (5) elucidate the mechanisms by which certain viruses (in particular Epstein-Barr virus) are able to transform cells and how chemical carcinogens may influence this expression; and (6) extrapolate (from accomplishing the above) to the understanding of human cancer.

Project Dates:

July 1984–June 1987.

Financial Support:

NCI (CA 36727).

1155. UNIVERSITY OF NEBRASKA MEDICAL CENTER, EPPLEY INSTITUTE FOR RESEARCH IN CANCER AND ALLIED DISEASES, 42nd and Dewey Avenue, Omaha, Nebraska 68105.

Project Title:

DNA Repair After Polycyclic Hydrocarbon Administration.

Principal Investigator:

Bresnick, E.

Objective:

To understand some of the factors that are responsible for the removal of deoxyribonucleoside adducts from DNA.

Methods or Approach:

Research is being conducted to determine the effects of benzo(*a*)pyrene on the alkaline elution profile of a cloned hamster tracheal cell line; the nature of the adducts; biological stability of adducts as altered by vitamin A analogs; and adduct occurrence in micrococcal nuclease-sensitive and nuclease-resistant portions of tracheal chromatin. Effects of asbestos and ability of vitamin A analogs to prevent any asbestos effects will be pursued. The enzyme system present in rat liver that is responsible for removal of O^6-methylguanine from methylated DNA will be purified and studies will be initiated of the repair enzymes involved in removal of deoxyguanosine-BaP and deoxyadenosine-BaP adducts from DNA alkylated with BaP diol epoxides. Liver and tracheal extracts will be employed.

Results to Date:

Available results have been published.

Future Plans:

Research will include (1) characterization of adducts by acid hydrolysis and separation of products by high performance liquid chromatography; (2) release of BaP tetrols; (3) modulation of glutathione levels in HTE-B cells; (4) quantification of topoisomerase levels in HTE-B cells; (5) influence of DNA polymerase inhibitors on repair of ultraviolet-induced DNA damage in HTE-B cells using alkaline elution technique; (6) influence of m-AMSA on repair of ultraviolet-induced DNA damage in HTE-B cells; (7) search for products of repair of BaP-damaged DNA in culture media; (8) purification of rat O^6-alkylguanine alkyltransferase; and (9) isolation of the human gene for O^6-alkylguanine alkyltransferase.

Project Dates:

April 1979–March 1986.

Financial Support:

NCI (CA 36679).

References:

(1) Bresnick, E. "The Price of Progress or Pandora's Purse." *Biochemical Pharmacology* 32:1331-1336, 1983. (2) Eastman, A.; Mossman, B.T.; Bresnick, E. "Influence of Asbestos on the Uptake of Benzo(*a*)pyrene and DNA Alkylation in Hamster Tracheal Epithelial Cells." *Cancer Research* 43:1251-1255, 1983. (3) Hora, J.F.; Eastman, A.; Bresnick, E. "O^6-Methylguanine Methyltransferase in Rat Liver." *Biochemistry* 22:3759-3763, 1983. (4) Ireland, C.M.; Eastman, A.; Bresnick, E. "The Influence of Inhibitors on the Repair of Benzo(*a*)pyrene Damaged DNA in Hamster Tracheal Epithelial Cells." *Carcinogenesis* 5:187-191, 1984. (5) Mossman, B.T.; Eastman, A.; Bresnick, E. "Asbestos and Benzo(*a*)pyrene Act Synergistically to Induce Squamous Metaplasia and Incorporation of ^{3}H-Thymidine in Hamster Tracheal Epithelium." *Carcinogenesis* 5:1401-1404, 1984. (6) Mossman, B.T.; Eastman, A.; Landesman, J.M., et al. "Effects of Crocidolite and Chrysotile Asbestos on Cellular Uptake and Metabolism of Benzo(*a*)pyrene in Hamster Tracheal Epithelial Cells." *Environmental Health Perspectives* 51:331-335, 1983.

1156. UNIVERSITY OF NEBRASKA MEDICAL CENTER, EPPLEY INSTITUTE FOR RESEARCH IN CANCER AND ALLIED DISEASES. 42nd and Dewey Avenue, Omaha, Nebraska 68105.

Project Title:
Polycyclic Hydrocarbon Metabolism and Carcinogenesis.

Principal Investigator:
Bresnick, E.
Objective:
To (1) study the characteristics of the initial complexation of 3-methylcholanthrene (3MC) to rat liver cytosolic protein; (2) investigate the nature of the nuclear acceptor; (3) purify the cytosolic protein to homogeneity; and (4) establish whether the cytochrome P450c genome is activated by quantitating the amount of P450c messenger RNA transcripts that are produced in an in vitro nuclear transcription system.
Methods or Approach:
Induction of cytochrome P450c, after administration of the polycyclic hydrocarbon 3MC to rats, would proceed in a manner analogous to the elaboration of certain estrogen-dependent proteins after exposure of target tissues to 17-estradiol. In the latter, 17-estradiol would bind with high affinity to a specific cytosolic receptor (the estrogen-bound receptor), after an activation reaction that occurs in the cytosol, would either transfer the ligand or ligand-receptor to an appropriate nuclear acceptor. This interaction leads to an increased transcription of the estrogen-dependent protein, e.g., ovalabumin.
Results to Date:
Results of research to date have been published.
Future Plans:
Specific aims will be to (1) purify the polycyclic aromatic hydrocarbon-binding protein from cytosol of rat liver; (2) characterize the protein in terms of its relationship to the TCDD-binding protein and determine the intracellular localization of the former; (3) determine if the ligand-bound binding protein can interact with specific regions of the cytochrome P450c gene (which has been isolated and sequenced); (4) establish the nature of the region of DNA to which the binding protein complexes; and (5) determine the mechanism of benzo(*a*)pyrene (BaP) and BaP phenol formation during microsomal metabolism of 6-nitrobenzo(*a*)pyrene.
Project Dates:
July 1982–June 1987.
Financial Support:
NCI (CA 36106-03).
References:
(1) Bresnick, E. "Prostaglandin Response in Mouse Skin to Tumor Promoters." *Prostaglandins and Cancer: First International Conference.* New York, Alan R. Liss, Inc., 1982, pp. 205-215. (2) Bresnick, E.; Foldes, R.; Hines, R. "Induction of Cytochrome P450 by Xenobiotics." *Pharmacological Reviews* 36:43S-51S, 1984. (3) Tierney, B.; Munzer, S.; Bresnick, E. "An Assay for the Detection of Specific Binding of 3-Methylcholanthrene to Rat Liver Cytosolic Proteins Using DEAE-Cellulose." *Analytical Biochemistry* 133:40-45, 1983. (4) Tierney, B.; Munzer, S.; Bresnick, E. "The Isolation and Characterization of Specific 3-Methylcholanthrene-Binding Proteins From Rat Liver Cytosol." *Archives of Biochemistry and Biophysics* 225:826-835, 1983.

1157. UNIVERSITY OF NEBRASKA MEDICAL CENTER, EPPLEY INSTITUTE FOR RESEARCH IN CANCER AND ALLIED DISEASES, 42nd and Dewey Avenue, Omaha, Nebraska 68105.

Project Title:
Epoxide Hydrolase in Normal, Hyperplastic and Neoplastic Livers

Principal Investigator:
Bresnick, E.
Objective:
To determine levels of epoxide hydrolase (EH) mRNA in livers of fetal, neonatal, weanling, and adult rats; in livers of animals treated with trans-stilbene oxide, phenobarbital, and 2-acetylaminofluorene (AAF); and in hyperplastic nodules and hepatomas that result following administration of AAF.
Methods or Approach:
Study data should provide information about the changes in EH mRNA during ontogeny, after administration of certain exogenous substances, during preneoplasia and hepatoma formation, and about the regulation of genomic DNA.
Results to Date:
Project is in a preliminary phase.
Future Plans:
Processing of nuclei precursor mRNA will be ascertained, and the ability of nuclei to transverse the EH mRNA under in vitro conditions will also be determined. Where this is found to be true, it will be established whether the mRNA transcription can be increased under these conditions. A full length cDNA will be produced, the DNA sequence of the full length cDNA will be determined, and a rat genomic library will be searched for EH gene information.
Project Dates:
March 1984–February 1987.
Financial Support:
NCI (CA 35994).

1158. UNIVERSITY OF NEBRASKA MEDICAL CENTER, EPPLEY INSTITUTE FOR RESEARCH IN CANCER AND ALLIED DISEASES, 42nd and Dewey Avenue, Omaha, Nebraska 68105.

Project Title:
Effect of Nitration on the Biological Effects of Benzo(*a*)pyrene.

Principal Investigator:
Bresnick, E.
Objective:
To prove the hypothesis that potentiation of biological activity by 6-nitro-benzo(*a*)pyrene (6-nitroBaP) is due to production of metabolites of 6-nitroBaP, some of which may be critical and react with cellular macromolecules, in particular DNA.
Methods or Approach:
Although air particulates collected from urban locations have been shown to contain bacterial mutagens and to induce malignant transformation in cultured mammalian cells, BaP content is not correlated with this biological activity. Under simulated environmental conditions, BaP and nitrogen oxides yielded 6-nitroBaP, which acts as an initiator in skin carcinogenesis. Sprague-Dawley rats will be induced with 3-methylcholanthrene, phenobarbital, and Arochlor 1254, and liver and lung microsomes will be prepared. In vitro metabolism with microsomes will be carried out and organic solvent-soluble metabolites of 6-nitroBaP will be identified to determine whether induction patterns make a difference in metabolite production. By using metyrapone and 1-benzylimidazole (inhibitors of cytochrome P450) and indomethacin (an inhibitor

of prostaglandin synthetase), it will be determined whether formation of some of the metabolites is susceptible to the inhibitors. Acrolein and mersalyl acid will be used to inhibit NADPH-cytochrome P450 reductase and to determine whether formation of some or all of the metabolites is inhibited. It has been reported that 3-hydroxy-b-nitroBaP is a metabolite, and a time-course study will determine whether phenols are formed as metabolites. The suggestion that in a nitro-hydrocarbon the nitro group may be replaced by hydrogen will be examined. Studies on intratracheal instillations of b-nitroBaP and BaP will be continued in female golden hamsters.

Results to Date:
Results are expected to make significant contributions to the understanding of the mechanisms by which 6-nitroBaP exerts its biological effects and also whether in vivo 6-nitroBaP is a carcinogen.

Project Dates:
July 1983–June 1985.

Financial Support:
Nebraska State Department of Health.

Reference:
Raha, C.; Hines, R.; Bresnick, E. "Demonstration of Microsomal Oxygenation of the Benzo-Ring of 6-Nitrobenzo(*a*)pyrene by Thin-Layer Chromatography." *Journal of Chromatography* 291:231-239, 1984.

1159. UNIVERSITY OF NEBRASKA MEDICAL CENTER, EPPLEY INSTITUTE FOR RESEARCH IN CANCER, Omaha, Nebraska 68105.

Project Title:
Binding of Aromatic Hydrocarbons to Nucleic Acids.

Principal Investigator:
Rogan, E.G.

Objective:
To determine structure of adducts formed between DNA and benzo(*a*)pyrene (BaP) in several biological systems, including an in vitro model system of horseradish peroxidase with hydrogen peroxide, which catalyzes one electron oxidation.

Methods or Approach:
Two target tissues will be analyzed for BaP-DNA adducts: mouse skin and rat mammary gland. ^{14}C-labeled BaP will be bound to DNA in the horseradish peroxidase/hydrogen peroxide binding system. DNA will be purified, digested enzymatically to deoxyribonucleosides, and analyzed by high pressure liquid chromatography. Mouse skin will be treated with ^{14}C-BaP by topical application and DNA will be purified and analyzed. Rat mammary gland will be treated by direct application of ^{14}C-BaP to gland area and DNA will be purified and analyzed. BaP-DNA adducts structures will be determined by cochromatography with model adducts of known structure prepared by anodic electrochemical oxidation of BaP in presence of deoxyribonucleosides. Structure of model adducts will be proven by UV absorbance spectra, fast atom bombardment mass spectrometry, and NMR. Cytochrome P-450, peroxidase, and prostaglandin H synthase activities will be assayed in mouse skin and rat mammary gland homogenates. Inhibitors of the various enzymes will be used and effect on yield of various adducts will be determined.

Results to Date:
Mouse skin DNA from animals treated with ^{14}C-BaP contains a major adduct with BaP bound at C-6 to an as yet unidentified position in deoxyguanosine. A second adduct also appears to have BaP bound at C-6 to another position in deoxyguanosine. These adducts are formed by one-electron oxidation, and constitute approximately as great a portion of BaP-DNA adducts as those formed from BaP bay region vicinal diolepoxide intermediates. DNA with BaP bound in horseradish peroxidase/hydrogen peroxide-catalyzed reaction contains at least one of these adducts with BaP bound at the 6 position to deoxyguanosine.

Future Plans:
The project will try to identify enzyme activities responsible for activation of BaP leading to binding to DNA and will generalize findings to other polycyclic aromatic hydrocarbons that have chemical properties suitable for activation by one-electron oxidation. It is anticipated that the predominant mechanism of activation in the mammary gland is one-electron oxidation catalyzed by some form of peroxidase.

Project Dates:
July 1979–December 1987.

Financial Support:
NCI (2R01CA25176).

1160. UNIVERSITY OF NEBRASKA MEDICAL CENTER, EPPLEY INSTITUTE FOR RESEARCH ON CANCER, Omaha, Nebraska 68105.

Project Title:
Cocarcinogenic Effect of Catechol in Rat Espohagus.

Principal Investigator:
Mirvish, S.

Objective:
To determine whether catechol in cigarettes contributes to esophageal cancer in rats.

Methods or Approach:
The hypothesis is tested by giving a nitrosamine to induce esophageal cancer in rats, together with catechol in the diet.

Results to Date:
A possible positive effect was found. Results have been submitted for publication.

Project Dates:
1980–1984.

Financial Support:
NCI (P01CA25100).

1161. UNIVERSITY OF NEBRASKA, LINCOLN, NEBRASKA PREVENTION CENTER FOR ALCOHOL AND DRUG ABUSE, Lincoln, Nebraska 68588-0137.

Project Title:
Long Term Evaluation of a Smoking Prevention Program for Grades 7 and 8.

Principal Investigators:
Newman, I.M.; Mohr, P.

Objective:
To design and evaluate a curriculum for grades seven and eight aimed at increasing knowledge about the immediate physiological effects of smoking and the pressures to smoke, and increasing students' assertiveness skills and abilities to refuse pressures to smoke.

Methods or Approach:
In the first year, half of approximately 1,200 to 1,500 students were taught the experimental curriculum and half served as controls. The curriculum was covered during seven class periods. All teachers received a day of special preparation for teaching the curriculum. A pretest was administered 1 week before the program started and a posttest was administered 2 to 3 weeks after completion of the curriculum. Followup data were gathered 1 year later. After the first cohort completed the curriculum, major revisions were made on advice of participat-

ing teachers. The second cohort of students is now receiving the revised curriculum.

Results to Date:

Using class means as the unit of analysis, a repeated ANOVA showed that experimental groups made significantly greater gains in knowledge than controls; however, items that attempted to measure a student's ability to say no and refuse direct pressures to smoke showed no differences between experimental and control groups. All students perceived themselves to be very capable, when necessary, of saying no and refusing direct pressures to smoke. A repeated measures ANOVA, using individual scores that tracked smokers and nonsmokers over time, showed that intentions "to be smoking in 5 years" decreased significantly for students in the first experimental group. An ANOVA was performed on 10 posttest-only items, which measured expectations of smoking in specific situations. Students who received the curriculum reported significantly less likelihood of smoking in the 10 situations than controls.

Project Dates:

June 1983–June 1985.

Financial Support:

Nebraska Health Department (85-47).

Nevada

1162. UNIVERSITY OF NEVADA, RENO, Psychological Service Center, Reno, Nevada 89557.

Project Title:

Social Network Influences in Smoking Cessation.

Principal Investigator:

Wood, Y.

Objective:

To explore the hypothesis that social networks can have a major impact on an individual's smoking behavior.

Methods or Approach:

Participants, recruited through the American Lung Association and newspaper advertisements, had to have made a serious attempt to quit smoking 3 to 6 months prior to participation. Interviews were conducted with 59 subjects (28 were abstinent and 26 had resumed smoking) to obtain smoking history and other background information. A participant's personal network consisted of people in the living situation, workplace associates, leisure time companions, and confidants. Smoking status (ex-smoker, smoker who tried to quit but relapsed) of network members was obtained and participants rated frequency with which network members engaged in 22 behaviors related to smoking.

Results to Date:

Preliminary analyses showed that smoking status of network members, including status of partner, was not significantly related to smoking status of the participant; however, behavior of members was related to participant's success in quitting. Positive reinforcement of effort, cooperative participation, and withholding of nagging/shunning or other punishing responses were highly related to positive (nonsmoking or reduced smoking) outcome. Behavior of network smokers was particularly important. Those who smoked in subject's presence or offered a cigarette appeared to have a significant negative impact, whereas smokers who avoided such activities and reinforced the participant's efforts appeared to be positive influences. Although the partner was a significant influence, results indicate that other individuals may have an even more powerful influence, particularly close friends, work associates, and "multidimensional" persons (those involved in two or more areas of the individual's life). Findings suggest that behavior of social network members needs further investigation to determine relationship to long-term smoking cessation. Current treatment programs may be able to increase effectiveness by addressing social network influences.

Future Plans:

Similar questions will be addressed in a prospective longitudinal design. The third phase will incorporate data from first and second phases in a treatment research project.

Project Dates:

September 1982–continuing.

Financial Support:

University of Nevada, Reno.

New Hampshire

1163. DARTMOUTH COLLEGE, DARTMOUTH MEDICAL SCHOOL, Department of Pathology, Hanover, New Hampshire 03756.

Project Title:

Pancreas and Liver Carcinogen Metabolism in Three Species.

Principal Investigator:

Curphey, T.J.

Objective:

To compare carcinogen metabolism and effects on DNA in pancreatic acinar cells, pancreatic duct cells, and liver cells from rats, hamsters, and humans.

Methods or Approach:

Methods include isolation and short-term culture of the three cell types from the three species. Carcinogen effects and metabolism were assessed by: (a) alkaline elution analysis of DNA damage; (b) autoradiographic and/or analytical demonstration of repair DNA synthesis in carcinogen treated cells; (c) binding of carcinogen to macromolecules of cell cytoplasm and nuclei; and (d) identification and quantitation of carcinogen metabolites in whole cells and subcellular fractions by HPLC and MS. Carcinogens studied include agaritine, the pyrrolizidine alkaloids, azaserine, N-nitrosobis(2-osopropyl)amine and related nitrosamines, dimethylnitrosamine, benzo(*a*)pyrene, and N^5-(N-methyl-N-nitrosocarbamoyl)-L-ornithine.

Results to Date:

Project has been completed but results are not yet available.

Project Dates:

September 1981–June 1984.

Financial Support:

NCI (R01 CA 30650).

1164. DARTMOUTH COLLEGE, DARTMOUTH MEDICAL SCHOOL, Department of Anatomy, Hanover, New Hampshire 03756.

Project Title:
Teratogenic Evaluation of Chronic Heavy Metal Exposure.

Principal Investigator:
Ferm, V.H.
Objective:
To determine the number of atoms of heavy metals required to produce a teratogenic event when the metal is administered under consistent and chronic conditions to pregnant animals in early gestation.
Methods or Approach:
Osmotic minipumps will be implanted into pregnant hamsters during early gestation. These pumps will contain concentrations of known teratogenic heavy metals (including cadmium). The teratogenic effect of these metals will be evaluated in later pregnancy and the specific teratogenic levels of chronic heavy metal exposure will be ascertained. In addition, the chemical status (free, protein-bound, etc.) of each heavy metal will be determined during the critical stages of embryogenesis.
Results to Date:
Project is in a preliminary phase.
Project Dates:
September 1982–1985.
Financial Support:
EPA (R810078-01-0).

1165. VETERANS ADMINISTRATION MEDICAL CENTER, 275 Chestnut Street, Manchester, New Hampshire 03103.

Project Title:
Interleukin-1 and Pulmonary Responses to Injury.

Principal Investigators:
Robins, A.G.; Hughes, S.L.
Objective:
To (1) confirm preliminary observations suggesting that cigarette smoking is associated with increased basal production of interleukin 1 (IL-1) by human pulmonary macrophages compared with cells from nonsmokers; (2) investigate the potential role of IL-1 administered locally to small animals on lung function and architecture; and (3) study pulmonary responses to common forms of injury such as infection.
Methods or Approach:
The investigations will determine what factors control IL-1 production in the respiratory tract. The question whether local IL-1 production has regional or systemic effects or both will be addressed. Effects of IL-1 production in the lung in response to injury will be studied.
Results to Date:
Project is in a preliminary phase.
Financial Support:
VA.

New Jersey

1166. BETH ISRAEL HOSPITAL, 70 Parker Avenue, Passaic, New Jersey 07055.

Project Title:
The Yearly Success Rate of Participants in the Smoking Cessation Clinic Entitled "Freedom From Smoking."

Principal Investigator:
Gorlick, B.
Objective:
To determine the success rate of participants in the "Freedom From Smoking" clinic who used nicotine gum compared with those who did not.
Methods or Approach:
The smoking cessation clinic, conducted through the lung association, consists of seven 1.5-hour behavior modification and education sessions and is available to communities and companies. Several companies are already participating. Followup will be conducted on a yearly basis.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–continuing.
Financial Support:
Beth Israel Hospital.

1167. U.S. ARMY COMMUNITY MENTAL HEALTH SERVICE, U.S. Army Medical Department Activity, Fort Dix, New Jersey 08640.

Project Title:
Three Session Smoking Cessation Through Hypnotic Suggestion.

Principal Investigator:
Klugman, P.J.
Objective:
To ascertain if a particular smoking cessation paradigm involving education, hypnotic suggestion, and training in self-hypnosis will be effective over time.
Methods or Approach:
A three-session smoking cessation program has been developed that involves a 1-hour educational session, a 2-hour hypnosis and self-hypnosis training session, and a 1-hour followup and reinforcement session. The sessions are to be conducted in a 1-week period with followup self-report questionnaires mailed after 1 week, 3 months, and 6 months. The study will be ongoing, including all subjects who present for smoking cessation. A running tabulation will be maintained of the percentage of individuals who have remained cigarette-free after each questionnaire period.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–continuing.
Financial Support:
DOD.

1168. KEAN COLLEGE OF NEW JERSEY, Department of Biology, Union, New Jersey 07083.

Project Title:
In Vitro Study of the Effect of Cigarette Smoke on the Viability of Oropharyngeal Bacteria.

Principal Investigator:
Bardell, D.

Objective:
To determine the effect of cigarette smoke on the viability of six species of normal oropharyngeal bacteria.

Methods or Approach:
Oropharygeal bacteria have considerable influence on their host. Normal oropharyngeal bacteria are beneficial, since invading pathogenic bacteria must compete with the established normal bacteria for a site of infection, whereas pathogenic bacteria cause diseases of the oropharyngeal cavity if invasion is successful. For this in vitro investigation, *Branhamella catarrhalis, Neisseria perflava,* and *Neisseria sicca* were studied as representative species of gram-negative bacteria commonly found in the oropharyngeal cavity of human beings. *Streptococcus salivarius, Streptococcus mitis* and *Streptococcus sanguis* were studied as representative species of gram-positive bacteria commonly found in the oropharyngeal cavity. Bacteria in culture medium at 37°C were subjected to eight puffs of smoke from one cigarette, and viable cell counts were done at intervals ranging from 0 min to 3 hr after exposure to smoke. The cigarette contained 23.0 mg of tar and 1.4 mg of nicotine. A popular brand of cigarettes, purchased locally, was employed. Each 25.0 ml puff of smoke from a mechanical smoking apparatus was passed over a 1.0 ml suspension of bacteria dispersed in a thin layer over a 25.0 cm^2 surface in a sterile flask. Filtered air was in contact with the suspension between puffs, and during the intervals between smoke treatment and viable cell counts being done. The methods and materials used in this in vitro study were devised to approximate conditions which exist when oropharyngeal bacteria of a smoker are exposed to cigarette smoke.

Results to Date:
There was a marked decrease in numbers of viable *Branhamella catarrhalis* at 15 min after exposure to smoke, and by 1 hr there were no viable cells in suspensions which originally contained 10^7 bacteria. No reduction in number of viable *Branhamella catarrhalis* occurred in an untreated suspension of the microorganism. There was a marked decrease in viable *Neisseria perflava* at 30 min, and by 3 hr there were no viable cells. There was a 4 to 5 $\log_{10}$ reduction of viable *Neisseria sicca* compared with untreated bacteria at 3 hr after exposure to smoke. *Streptococcus mitis, Streptococcus salivarius,* and *Streptococcus sanguis* were less susceptible to the harmful action of cigarette smoke, and by 3 hr there were 1 to 2 $\log_{10}$ differences in viable cell counts between smoke-treated and untreated bacteria. Non-filter cigarette smoke had a greater detrimental effect on all species of bacteria studied than smoke from filter-tipped cigarettes.

Future Plans:
The three species of gram-negative oropharyngeal bacteria studied were more susceptible to the toxic action of cigarette smoke than the three species of gram-positive oropharyngeal bacteria studied. Therefore, additional species will be studied to determine if gram-negative bacteria are characteristically more susceptible to the harmful action of cigarette smoke than gram-positive bacteria. The action of some individual constituents of cigarette smoke on the viability of oropharyngeal bacteria will also be investigated.

Project Dates:
September 1978–continuing.

Financial Support:
Kean College of New Jersey; New Jersey State Department of Higher Education.

References:
(1) Bardell, D.; Smith, J.E. "An In Vitro Study of the Exposure of Mixed Populations of Normal Oropharyngeal Bacteria to Cigarette Smoke." *Microbios* 26:159-164, 1979. (2) Bardell, D. "Viability of Six Species of Normal Oropharyngeal Bacteria After Exposure to Cigarette Smoke In Vitro." *Microbios* 32:7-13, 1981.

1169. KEAN COLLEGE OF NEW JERSEY Department of Biology, Union, New Jersey 07083.

Project Title:
In Vitro Exposure of Adenovirus Types 5 and 7 in Oropharyngeal Secretions to Cigarette Smoke.

Principal Investigator:
Bardell, D.

Objective:
To determine whether cigarette smoke has a deleterious effect on adenovirus type 5 (nononcogenic) and type 7 (oncogenic).

Methods or Approach:
Viruses, the most frequently found etiological agents of infectious respiratory tract diseases, are present in oropharyngeal secretions or adhere to cells or other oropharyngeal cavity surface structures that are in the pathway of cigarette smoke during inhalation and exhalation. There are at least 35 known antigenic types of andenoviruses that infect human beings, with upper respiratory infections being the most common. Adenovirus types 5 and 7 were suspended in clarified oropharyngeal secretions. After 1.0 mL of suspension was dispersed in a thin layer over a 25 cm^2 surface in a flask, the suspension was exposed at 37° C to eight 25 mL puffs of smoke from one cigarette, using a mechanical smoking apparatus. Nonfilter cigarettes contained 23 mg tar and 1.4 mg nicotine; filter cigarettes, 19 mg tar and 1.2 mg nicotine. Smoke was flushed from the flask with normal filtered air. At 0, 15, and 60 minutes after exposure to smoke, untreated and smoke-treated viruses were titrated using monolayer cultures of human epithelioid (HEp-2) cells. Normal air was in contact with the suspensions between puffs of smoke and between smoke treatments and virus titrations.

Results to Date:
Smoke from filter and nonfilter cigarettes had no effect on infectivity and replication of adenovirus types 5 and 7. Smoke from four cigarettes administered over a 4-hour period caused a 2 to 3 $\log_{10}$ drop in titer of both viruses. However, smoke from four cigarettes was highly toxic for HEp-2 host cells of the viruses and was more harmful to host cells than to the viruses. Therefore, results indicate that the amount of smoke required to inactivate adenoviruses would probably be more harmful to epithelial cells lining the respiratory tract than to viruses located in the tract.

Future Plans:
The effect of cigarette smoke on other viruses and on bacteria found in the upper respiratory tract of human beings will be investigated.

Project Dates:
September 1978–continuing.

Financial Support:
Kean College of New Jersey; New Jersey State Department of Higher Education.

Reference:
Bardell, D. "In Vitro Exposure of Adenovirus Types 5 and 7 in Oropharyngeal Secretions to Cigarette Smoke." *Applied and Environmental Microbiology* 45:770-773, 1983.

1170. MEDICAL CONTROL CENTERS, 200 Engle Street, No. 10, Englewood, New Jersey 07631.

Project Title:
Effects of Multiple Smoking Cessation Methods on Subpopulations of Smokers.

Principal Investigators:
Bars, M.P.; Smithbauer, W.G.
Objective:
To determine which smoking cessation methods or combination of methods are most effective with different types of smokers.
Methods or Approach:
Smokers enrolled in a multimodal commercial smoking cessation program will be categorized on the basis of standard classification criteria including Horn's Smoker's tests, the Fagerstrom Index, and other behavioral, sociological, demographic, and personality measures. Using factor analysis and other statistical methods, an attempt will be made to determine which smoking cessation methods or combination of methods (psychological, group therapy, relaxation exercises, pharmacological, acupuncture, etc.) are most effective with different smoker subpopulations.
Results to Date:
Project is in a preliminary phase.
Project Dates:
July 1985–continuing.
Financial Support:
Medical Control Centers Inc.

1171. NEW JERSEY MEDICAL SCHOOL, 100 Bergen Street, Newark, New Jersey 07103. SETON HALL UNIVERSITY, South Orange, New Jersey 07079.

Project Title:
Worksite Risk Reduction.

Principal Investigators:
Lasser, N.; Levy, J.C.
Objective:
To evaluate effects of a comprehensive educational self-help program on health practices, attitudes and knowledge; determine changes in cigarette smoking, blood pressure, and serum cholesterol.
Methods or Approach:
A quasi-experimental pretest–posttest design is being employed at two comparable worksites.
Results to Date:
Project is in a preliminary phase.
Project Dates:
November 1984–December 1987.
Financial Support:
AHA.

1172. NEW JERSEY STATE DEPARTMENT OF HEALTH, CANCER EPIDEMIOLOGY SERVICES UNIT, CN 360, Trenton, New Jersey 08625.

Project Title:
Retrospective Case–Control Studies of Lung Cancer in New Jersey.

Principal Investigators:
Stemhagen, A.; Altman, R.; Schoenberg, J.
Objective:
To (1) identify risk factors associated with lung cancer in New Jersey; (2) evaluate occupational exposures and their association with cigarette smoking; and (3) assess the role of Vitamin A in the development of lung cancer.
Methods or Approach:
Two retrospective case–control studies are being conducted. The first includes 1,000 male lung cancer cases and 1,000 population-based controls in six geographic areas of New Jersey. These areas have historically shown significantly high lung cancer mortality rates for males. The second study involves 900 female lung cancer cases and 900 population-based controls. Female respondents were identified statewide. All lung cancer cases must be pathologically confirmed. All information was obtained by personal interview of study subjects or their next of kin.
Results to Date:
Interviews with all cases and controls have been completed. Data analyses are ongoing.
Project Dates:
December 1980–June 1984.
Financial Support:
NCI (N01 CP-61031).

1173. RUTGERS MEDICAL SCHOOL, Department of Medicine. St. Peter's Medical Center, 254 Easton Avenue, New Brunswick, New Jersey 08903.

Project Title:
Topics in the Treatment and Prevention of Tobacco Use.

Principal Investigator:
Slade, J.D.
Objective:
To develop a culturally based model of tobacco use; develop treatment and prevention strategies that emerge from the model.
Methods or Approach:
Data are being collected that explore the hypotheses that social, political, cultural, and economic forces participate in initiating and sustaining tobacco use. Literature searches, observations, and questionnaire surveys have been employed.
Results to Date:
Data are consistent with the hypothesis that cultural forces and the cultural climate are important initiating and sustaining factors in tobacco use. Whether thesse observations will lead to specific methods for treatment and prevention remains to be determined.
Project Dates:
November 1983–continuing.
Financial Support:
Rutgers Medical School.
Reference:
Slade, J.D. "A Disease Model of Cigarette Use." *New York State Journal of Medicine* (In press).

1174. RUTGERS UNIVERSITY, Department of Chemistry, Wright-Rieman Laboratories, New Brunswick, New Jersey 08903.

Project Title:
Carcinogens by Hydrocarbons: A Molecular Approach.

Principal Investigator:
Olson, W.K.
Objective:
To elucidate the unique three-dimensional (conformational) features of nucleic acids modified by selected carcinogens; comprehend configuration-dependent properties of these complex systems in terms of basic chemical structure and conformation.
Methods or Approach:
Research is divided into three interrelated stages: (1) theoretical potential energy calculations of carcinogen-modified nucleic acid conformation; (2) statistical mechanical studies to test validity of energy predictions; and (3) computer model building of likely three-dimensional structures.

Results to Date:
Covalent binding of various carcinogens, such as benzo(*a*)pyrene, to nucleic acid bases appears to force these aromatic units from their normal antiorientation (directed into the core of the DNA double helix) into a synarrangement directed toward the surface of the structure. In turn, this glycosyl change perturbs the attached sugar and adjacent phosphate groups. The sugar rings of modified units are apparently free to pseudorotate over their pathways of puckered forms and the populations of the exocyclic bond rotations are shifted to different local conformational ranges. Calculations have also provided insight into the ways in which the syn–anti conformational conversion can be achieved. Syn–anti transitions sometimes occur within the confines of a polynucleotide helix without perturbing normal Watson-Crick hydrogen bonding. In such events, sugars reorient with respect to base units. Glycosyl changes associated with mispairing of bases, however, require open arrangements analogous to those required for normal DNA "breathing" and intercalation. The base then reorients with respect to the sugar–phosphate backbone. The presence of intercalants at the opening sites, however, prevents the syn-anti interconversion.
Project Dates:
September 1979–continuing.
Financial Support:
Rutgers University, Wright-Rieman Laboratories

1175. RUTGERS UNIVERSITY, GRADUATE SCHOOL OF SOCIAL WORK, 536 George Street, New Brunswick, New Jersey 08903.

Project Title:
Comparative Health Measures: The Relationship Between Self Perceptions of Health and Clinical/Medical Health in a Population of Poor, Urban, Elderly Blacks.

Principal Investigator:
Ross, R.E.
Objective:
To (1) describe health of the sample population; (2) test efficiency of self-perceived health as a more readily accessible indicator of clinically/medically assessed health; (3) describe relationship among several self-perceived health measures and medically/clinically assessed health measures; (4) determine degree of congruence between self-perceived health and medical condition of respondent (determined by physician or clinical methods); (5) examine association of self-perceived health and clinically/medically assessed health measures and respondents' view of themselves as aging persons; (6) describe effects of demographic variables (sex, age, previous occupation, education, marital status, current living arrangement, current income) with health measures; and (7) describe effects of psychosocial variables, including weekly activity level; knowledge of community resources; role of religion; respondent's ratings of moods; respondent's ratings of ability to manage on available income; and global happiness and life satisfaction.
Methods or Approach:
The cross-sectional, descriptive study of two related and combined panels is extracted from a larger, longitudinal research project. Panels were randomly selected from oversampled census in a catchment area census district in an inner city area. Face to face interviews, physician's exams, and other medical data are sources. Cross tabulation, t-tests, Pearson, and partial correlation were used in analysis. Measure of smoking was in the form of a three-way variable: smoking now, stopping smoking, or never smoked. Information was compared with demographic and health measures.

Results to Date:
No relationship was found between smoking and any of the clinical/medical or self-perceived health measures. Smoking was related to sex and age of respondent; greater numbers of younger respondents (aged 50 to 64 years) still smoke while greater numbers of middle-aged respondents (aged 65 to 74 years) have quit. A greater number of those aged 75 or over never smoked. More men than women still smoke, more women than men never started smoking, and equal numbers have quit. Smoking played only a small role in this urban, elderly, black population, where tobacco users were largely chewers or snuff-dippers, many of whom could not afford cigarettes at the appropriate time.
Project Dates:
September 1983–September 1984.
Financial Support:
NCHSR (HS 05037).

1166. UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY, NEW JERSEY MEDICAL SCHOOL, 100 Bergen Street, Newark, New Jersey 07103.

Project Title:
Clean Indoor Air Laws and Male/Female Smoking Differences

Principal Investigators:
Lewit, E.M.; Wooley, B.; Shakotko, R.
Objective:
To further the understanding of cigarette smoking; contribute to formulation of policies conducive to control of smoking.
Methods or Approach:
Multivariate statistical techniques are used to investigate the effects of laws that restrict cigarette smoking (clean indoor air laws). Information contained in the National Surveys on Drug Abuse (NSDA) and the Health Interview Surveys (HIS) are used to determine (1) whether legal smoking restrictions cause smokers to reduce the number of cigarettes smoked; (2) whether the laws encourage or facilitate quitting; and (3) whether the laws discourage initiation of smoking. A second project will explore differences and similarities in factors affecting smoking by males and females during the 1970s, using data from the NSDA and HIS. Multivariate techniques will be used to determine the extent to which differences in smoking by sex may be attributed to sex-specific differences in response to exogenous factors, levels of the exogenous factors, sex-specific differences in levels of exogenous factors, and extent to which apparent difference in response to the antismoking campaign by men and women may be attributed to differences in trends in underlying factors.
Results to Date:
Results are not yet available.
Project Dates:
January 1984–January 1985.

1177. VETERANS ADMINISTRATION MEDICAL CENTER, Tremont Avenue and South Center Street, East Orange, New Jersey 07019.

Project Title:
Tracheobronchial Tree. Histologic Findings in Bronchial Epithelium.

Principal Investigators:
Auerbach, O.; Garfinkel, L.
Objective:
To test the hypothesis that the reduction in tar and nicotine

content of cigarette smoke that began in the 1950s should be reflected by histologic changes in the bronchial epithelium of cigarette smokers.

Methods or Approach:

Microscopic examinations (random order) of 20,424 sections from the bronchial tubes taken at autopsy of 445 men (non-lung cancer deaths) were made. There were 211 men who died between 1955 and 1960, of whom 154 smoked regularly; and 234 who died between 1970 and 1977, of whom 181 were regular smokers. Changes studied included basal cell hyperplasia, loss of cilia, and occurrence of cells with atypical nuclei.

Results to Date:

In both periods studied, histologic changes occurred far less frequently in nonsmokers than in cigarette smokers and increased in frequency with amount of smoking, adjusted for age. Sections with advanced histologic changes in those dying in 1955-1960 occurred in 0 percent of nonsmokers, in 2.6 percent of those smoking 20 to 39 cigarettes/day, and in 22.5 percent of those smoking >40 cigarettes/day. In those who died in 1970-1977, the percentages were 0, 0.1, 0.8, and 2.2, respectively.

Future Plans:

Specimens of the tracheobronchial tree, still being collected, will be used in anticipated future studies.

Project Dates:

1970–continuing.

Financial Support:

VA (11-0592).

Reference:

Auerbach, O.; Garfinkel, L. "Changes in Bronchial Epithelium in Relation to Cigarette Smoking." *New England Journal of Medicine* 300:381-386, 1979.

1178. VETERANS ADMINISTRATION MEDICAL CENTER, Tremont Avenue and South Center Street, East Orange, New Jersey 07019.

Project Title:

Effect of Variation in Tar and Nicotine Content of Cigarettes in Smoking Dogs. Second Study.

Principal Investigators:

Auerbach, O.; Garfinkel, L.; Romig, P.L.

Objective:

To study cigarette exposure in relation to tar and nicotine content of cigarettes and the relationship to pathologic changes.

Methods or Approach:

Smoke inhalation studies were conducted using beagle dogs. On the basis of findings in animal studies, available human material was reviewed.

Results to Date:

Findings showed less damage to lungs of dogs smoking cigarettes with an efficient filter than in dogs smoking cigarettes without filters. It is concluded, from smoke inhalation studies conducted over a 15-year period, that there has been a decrease in changes in the lungs, heart, and tracheobronchial tree of dogs in more recent studies than were present in the first smoking study. These changes are in the degree of pulmonary fibrosis and emphysema, basal cell hyperplasia of the bronchial epithelium with atypism, coronary arteriosclerosis, and development of pulmonary embolism. Smoke inhalation studies using beagle dogs have added much to this knowledge. Findings in human studies were similar.

1179. VETERANS ADMINISTRATION MEDICAL CENTER, Tremont Avenue and South Center Street, East Orange, New Jersey 07019.

Project Title:

Early Morphologic Changes in the Distal Respiratory System of Smoking Dogs.

Principal Investigators:

Auerbach, O.; Frasca, J.M.; Carter, H.W.

Objective:

To determine early morphological changes in lungs of beagle dogs exposed to cigarette smoke and how such changes are related to the development of emphysema.

Methods or Approach:

Pulmonary fibrosis and emphysema were produced in beagle dogs by direct inhalation of cigarette smoke over a relatively short period of time. One dog was sacrificed after inhaling smoke from 172 cigarettes, one after 282 cigarettes, and others after 480 and 534 cigarettes, respectively.

Results to Date:

Examination of the lungs by scanning and transmission electron microscopy showed a range of response, from the presence of numerous smoker's macrophages to extensive alterations including destruction and enlargement of alveolar ducts and varying degrees of enlargement of alveolar spaces. Interalveolar pores were enlarged and marked fenestration leading to destruction of the alveolar walls became apparent. Features were accompanied by interstitial fibrosis of the interalveolar septa. No evidence of chronic bronchitis and/or bronchiolitis or of physical obstruction to the terminal airways was found in the early development of fibrosis and emphysema.

Financial Support:

VA.

Reference:

Frasca, J.M.; Auerbach, O.; Carter, H.W., et al. "Morphologic Alterations Induced by Short-Term Cigarette Smoking." *American Journal of Pathology* 111:11-20, 1983.

1180. VETERANS ADMINISTRATION MEDICAL CENTER, Tremont Avenue and South Center Street, East Orange, New Jersey 07019.

Project Title:

Inhalation Bioassay of Cigarette Smoke in Male Beagle Dogs.

Principal Investigators:

Auerbach, O.; Romig, P.L.; Frasca, J.M., et al.

Objective:

To study the effects of high-tar/high-nicotine (HN), medium-tar/medium-nicotine (MN), and low-tar/low-nicotine (LN) cigarettes in the development of pulmonary and cardiovascular diseases in male beagle dogs chronically exposed to cigarette smoke.

Methods or Approach:

The 117 dogs studied were divided into the following four groups: 37 HN dogs, 29 MN dogs, 33 LN dogs, and 18 control (sham-smoked) dogs. Over the study period, animals smoked from 6,488 to 8,960 cigarettes for from 627 to 833 days. Autopsies were performed and sections were prepared for microscopic examination.

Results to Date:

Changes among the three smoking groups varied. The HN group showed more changes than the MN group, which showed more changes than the LN group. In the HN group, there was more advanced pulmonary fibrosis and emphysema than in the other two groups. There was more basal cell hyperplasia and more atypism in the tracheobronchial epithelium in the HN group than in the MN group and more in the MN group than in the LN group. In addition to the variation in the degree of changes, squamous metaplasia of the tracheobronchial epithelium was more frequent and showed more atypical changes in the HN group than in the MN group. The MN group showed more evidence of squamous metaplasia than the LN group. Final results indicate that changes resulting from cigarette smoking (squamous metaplasia with atypism, pulmonary fibrosis and emphysema, bronchioalveolar tumors with minimal atypism and minimal squamous metaplasia) occurred less frequently in this group of dogs than in any studied in earlier research.

Financial Support:
VA.

1181. VETERANS ADMINISTRATION MEDICAL CENTER, Tremont Avenue and South Center Street, East Orange, New Jersey 07019.

Project Title:
Techniques for Early Detection of Oral Carcinoma.

Principal Investigator:
Mashberg, A.

Objective:
To (1) determine the earliest visual signs of asymptomatic squamous carcinoma of the oral cavity and pharynx; (2) evaluate toluidine blue as a simple diagnostic modality via direct application or rinse to detect presence of asymptomatic oral carcinoma (TIS or TI); (3) assess significance of alcohol as a risk factor in development of oral and pharyngeal squamous carcinoma; and (4) determine incidence of second primaries of the upper aerodigestive tract and lung in patients with index oral carcinoma.

Methods or Approach:
Patients with persistent mucosal changes of the oral cavity will be accessioned, tentative clinical diagnoses will be made, and lesions will be stained with toluidine blue application and toluidine blue rinse. Biopsies of lesions will be performed and comparative studies will be conducted to determine false negatives and positives (i.e., specificity and sensitivity), for impressions based on clinical criteria, toluidine blue application, and toluidine blue rinse compared with final pathological diagnosis. Cancer cases will be compared with controls from the identical population to determine significance of alcohol and cigarette smoking as risk factors. Patients will be interviewed after lesions are identified as carcinoma. Controls (without carcinoma) who are patients in same clinical setting will be interviewed concerning demographic habits. Incidence of second primaries of the aerodigestive tract will be determined by followup, chart evaluation, and tumor registry. This research is highly relevant in VA populations since patients are at risk for oral, pharyngeal, and upper aerodigestive carcinomas, presumably related to heavy cigarette smoking and alcohol intake. Developing new and more specific criteria for asymptomatic lesions and a diagnostic test to detect innocuous or undetected lesions is of importance to patient care and survival, since most patients treated for oral and pharyngeal carcinoma are already asymptomatic Stage III-IV with poor prognosis. High incidence of second aerodigestive primaries suggest using the index oral lesion as a "flag" to identify patients at risk.

Results to Date:
Erythroplasia in high risk sites (ventrolateral tongue, floor of the mouth, and soft palate complex) has been established as the earliest visual sign of oral and pharyngeal carcinoma. Toluidine blue application and rinse are effective diagnostic procedures for detection of asymptomatic carcinoma. Over 90 percent sensitivity and specificity has been documented, and a patent for the toluidine blue rinse has been awarded. Oral cancer is being used as a marker or flag indicating the possible presence of a second cancer of the upper aerodigestive tract, since about 30 percent of patients have another primary in these areas. Case-control studies related to alcohol and tobacco as risk factors in oral and pharyngeal cancer are continuing. Preliminary findings suggest that heavy alcohol intake may be a greater risk factor than smoking in this population.

Financial Support:
VA.

1182. VETERANS ADMINISTRATION MEDICAL CENTER, Tremont Avenue and South Center Street, East Orange, New Jersey 07019.

Project Title:
Oral Cancer - Risk for Upper Aerodigestive and Lung Primaries.

Principal Investigators:
Mashberg, A.; Rush, B.F.; Grossman, M.L., et al.

Objective:
To collect, analyze, and report data that relate to development of synchronous and metachronous primary cancers of the upper aerodigestive tract (hydropharynx, larynx, esophagus) and lung in patients initially diagnosed as having an index squamous cancer of the oral cavity or oropharynx (cases).

Methods or Approach:
Differences in frequency of upper aerodigestive and lung primaries in over 400 cases and 2,476 controls will be compared, and the relative risk of cases developing a new primary of the upper aerodigestive tract and lung will be determined. Additionally, relative risk related to smoking and drinking will be compared to determine effect on development of other primary cancers in cases vs. development of primary cancers in controls. Tumor Registry, Veterans Administration Medical Center, and New Jersey Department of Health records will be evaluated with previously obtained demographic data. If the high frequency of multiple primaries in cases is confirmed and relative risk for developing new primaries is greater for those with an index oral cancer, it is proposed that the index oral cancer may serve as a "flag" to identify patients who are prone to develop multiple cancers. Identification of patients at risk would mandate further diagnostic studies for detection of other primaries at time of identification of index oral lesions and in followup programs. It is anticipated that earlier identification of new primaries of the upper aerodigestive tract and lung prior to development of obvious symptomatology may increase survival. Also, if the high relative risk of drinking and cigarette smoking for developing aerodigestive cancer in cases vs. controls is ascertained, it would further support the hypothesis that squamous carcinoma is not an isolated disease of one anatomical site, but a field, regional, or systemic disease entity mandating an alteration in the present concept of ablative therapy, i.e., the ablative modalities of surgery and radiotherapy for the single oral or pharyngeal manifestation are insufficient, and appropriate studies in regional or systemic treatments for head and neck and upper aerodigestive tract carcinoma may be necessary to develop more effective treatment.

Results to Date:
Results are not yet available.

Financial Support:
VA.

1183. VETERANS ADMINISTRATION MEDICAL CENTER, Tremont Avenue and South Center Street, East Orange, New Jersey 07019.

Project Title:
Alcohol in Non-Cigarette Smokers as a Primary Risk Factor in Oral and Pharyngeal Carcinoma - A Study in the City of Turin, Italy.

Principal Investigators:
Mashberg, A.; Merletti, F.D.; Terracini, B.
Objective:
To investigate the association of alcohol, tobacco, and occupation with cancer of the oral cavity and orophaynx; study the interaction between alcohol and tobacco in oral carcinogenesis in a population who drink heavily, but where a relatively large proportion of drinkers do not smoke.
Methods or Approach:
New cases among residents of the city of Turin and a random sample of the general population are being interviewed. Oral and pharyngeal cancer cases are recruited in 14 hospital wards and represent at least 90 percent of cases in the population under study. Interviews record lifetime occupational history and current and past tobacco and alcohol consumption. Sixty new cases are expected yearly. Statistical analysis of data will be made with particular attention to the role of alcohol in nonsmokers and the specific role of wine as a risk factor. Previous studies indicate cigarette smoking and alcohol to be significant risk factors in oral and pharyngeal cancer and suggest that doubling alcohol consumption increases risk more than doubling cigarette consumption, and that beer and wine are greater risk factors than whiskey. If the independent risk of alcohol can be ascertained in this population with a proportion of nonsmoking drinkers, it will clearly establish the role of alcohol as a risk factor and suggest the importance of clinical measures to restrict alcohol consumption.
Results to Date:
To date, approximately 80 cases have been identified; a total of 120 cases is expected by the end of 1984.
Financial Support:
VA.

1184. VETERANS ADMINISTRATION MEDICAL CENTER, Tremont Avenue and South Center Street, East Orange, New Jersey 07019.

Project Title:
Epidemiologic and Laboratory Studies of Oral and Oral Pharyngeal Squamous Carcinoma in a Bi-Racial Veterans Population.

Principal Investigators:
Mashberg, A.; Hoffman, D.
Objective:
To correlate lesions in the oral cavity with epidemiological and biochemical findings; establish indicators for high risk of oral cavity and pharyngeal cancer in males in the United States.
Methods or Approach:
Comparison of biochemical data from patients vs. controls should allow distinction of factors that are correlated with the disease. Measurements and comparisons may also serve to indicate whether gradual changes of certain parameters in physiological fluids concur with gradual advances from a nondiseased oral cavity to severe dysplasia, carcinoma in situ, and ultimately, invasive squamous carcinoma. Biochemical indicators can also be used to validate questionnaire information with respect to smoking habits. It is planned to evaluate 180 patients with oral or oral pharyngeal cancer and 540 controls from a Veterans Administration medical center. At time of diagnosis, patients will be interviewed and samples of saliva, blood, and urine will be collected. Saliva samples will be analyzed for nitrate, nitrite, thiocyanate (SCN), nicotine (NIC), cotinine (COT), tobacco-specific N-nitrosamines (TSNA), zinc (Zn), and ascorbic acid (AA). Blood will be analyzed for SCN, NIC, COT, Zn, carboxyhemoglobin, AA, carotenes, vitamin E, vitamin B_2, and selenium. NIC, COT, pH, Zn, N-nitrosoproline, and creatinine will also be determined in urine.
Results to Date:
Results are not yet available.
Financial Support:
VA.

1185. VETERANS ADMINISTRATION, 379 Tremont Avenue, East Orange, New Jersey 07018.

Project Title:
The Role of CEA Assay in the Diagnosis, Therapy, and Follow-Up of Head and Neck Carcinoma.

Principal Investigators:
Cheung, N.K.; Serlin, O.; Rush, B.F., et al.
Objective:
To (1) determine the correlation of carcinoembryonic antigen (CEA) titers with diagnosis of head and neck carcinoma; (2) study the effect of radiotherapy on the CEA titer in treatment of head and neck carcinoma; and (3) assess the usefulness of the CEA titer in the long-term followup and management of head and neck carcinoma.
Methods or Approach:
Ten consecutive patients admitted to the hospital with newly diagnosed head and neck carcinomas will be admitted to the study. Patients known to have other active malignant disease at the time of admission and with severe hepatic disease will be excluded. Approximately 10 mL of each patient's blood will be drawn into a Vacutainer tube with liquid EDTA. The specimen will be drawn carefully to avoid hemolysis and will be centrifuged, separating plasma within 6 hours of venipuncture. The assay may be done by any laboratory, but should be the CEA Roche methodology. Specimens for the CEA assay will be drawn from patients receiving radiotherapy prior to surgical procedures as follows: (1) at the time of diagnosis; (2) after 3 weeks of radiation therapy; (3) at the end of radiation therapy; (4) 6 weeks later, just before surgery; (5) 2 weeks post-op; (6) 1 month post-op; (7) 3 months post-op; and (8) 6 months post-op. Patients going directly to surgery without radiotherapy will begin just before surgery. Patients receiving neither radiotherapy nor surgery will have the speciman drawn at the time of diagnosis.
Results to Date:
CEA titers were studied in 20 patients with advanced head and neck carcinoma. These patients had a history of excessive alcoholic intake and cigarette smoking. Contrary to previous studies, most of these patients had very low CEA titers. Patients with very early stages of squamous carcinoma within the head and neck area were also studied. Their CEA titers were again in the low range. It is concluded that CEA titers may not be a sensitive marker for monitoring patients with head and neck carcinoma.
Financial Support:
VA.

1186. VETERANS ADMINISTRATION, 379 Tremont Avenue, East Orange, New Jersey 07018.

Project Title:
Testicular Androgen Hydroxylases: Hormonal and Drug (Dioxin) Effects.

Principal Investigators:
Mittler, J.C.; Ertel, N.H.

Objective:
To determine whether or not pubertal changes in testicular morphology, chronic smoking, and/or exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) alter androgen hydroxylases in the testis (and presumably alter the metabolic fate of testosterone).

Methods or Approach:
Whole testes, isolated interstitial cells, and seminiferous tubules from rats of varying ages or after TCDD exposure were obtained. Testes from dogs that had smoked cigarettes for approximately 2 years were also obtained. Microsomal preparations from these animals were assayed for β-hydroxylase, 7α-hydroxylase, 16α-hydroxylase, 5α-reductase, 3α-ol-dehydrogenase, and 3β-ol-dehydrogenase activity on testosterone. Tritiated steroids were extracted from incubation media, isolated by thin layer chromatography, and counted by liquid scintillation. Data were normalized to the protein content of the various microsomal preparations. Identity of the various steroids was confirmed by multiple chromatographies and by recrystallization. Also, further metabolism of the steroids was assessed.

Results to Date:
With puberty, production of 7α-hydroxytestosterone rose markedly in both seminiferous tubules and interstitial cells. It was reduced in the whole testes of dogs that were heavy smokers. Such dogs had prostates only 44 percent of normal size ($p<0.001$). 7α-Hydroxylase activity was not affected by TCDD. Smoking stimulated the 6β-hydroxylase in liver (but not in testes) and reduced serum testosterone levels. Serum luteinizing hormone was elevated in smoking dogs. TCDD stimulated 6β-hydroxylase activity in interstitial cells, but not in seminiferous tubules. TCDD stimulated the 16α-hydroxylase in both seminiferous tubules and interstitial cells. This work may eventually influence the diagnostic approaches to infertility and perhaps treatments and may also influence research on contraception.

Financial Support:
VA.

New Mexico

1187. LOS ALAMOS NATIONAL LABORATORY, P.O. Box 1663, MS K404, Los Alamos, New Mexico 87545.

Project Title:
Human Health Effects of Plutonium.

Principal Investigators:
Wilkinson, G.S.; Wiggs, L.D.; Voelz, G.L.

Objective:
To (1) investigate whether adverse health effects are associated with exposures to plutonium; (2) explore the health effects of exposure to other radioisotopes, transuranic elements, and hazardous substances found in nuclear facilities using plutonium; and (3) describe the nature of such health effects should they be discovered.

Methods or Approach:
Mortality and disease are examined among workers exposed to plutonium at six study sites: Los Alamos (New Mexico), Rocky Flats (Colorado), Hanford (Washington), Mound (Ohio), Savannah River (South Carolina), and Oak Ridge (Tennessee). Standardized mortality ratios will be computed with expected numbers based on county, state, and national mortality rates. Comparisons of exposed and nonexposed subcohorts of workers will also be made. Since 1952, 26 plutonium workers exposed between 1944 and 1945 at Los Alamos have been followed clinically at approximately 5-year intervals. Since 1974, 241 workers with a history of high exposures have been followed by health questionnaire. Information on smoking has been collected to study possible effects of inhaled plutonium particles in smokers compared with nonsmokers.

Results to Date:
Data on smokers among the 241 plutonium-exposed Los Alamos workers do not support a hypothesis that the risk of lung cancer is higher among smokers exposed by inhalation to plutonium particles than in smokers not so exposed. Standardized mortality ratios, adjusted for age and calendar year of death for white males employed at Rocky Flats, do not demonstrate excess mortality from all causes or all cancer, including cancers of special interest (bone, liver, lung, or lymph and hematopoietic systems). An excess of brain tumors was observed among the cohort of white males employed 2 or more years and among the subcohort exposed to ≥ 1 rem external radiation, an excess not observed among the plutonium-exposed subcohort. A subsequent case–control study of brain tumors among this cohort found no statistically significant associations between brain tumor death and exposure to internally deposited plutonium, external radiation, or other occupational risk factors. Mortality data for the two special study groups at Los Alamos do not demonstrate excess mortality from all causes or all cancer, including those of special interest.

Future Plans:
Mortality analyses for study populations will continue. A major study focus will be surveillance of incidence of selected diseases, which is expected to continue through the year 2000, to compare rates for plutonium-exposed vs. unexposed cohorts. Significant associations found in either mortality or incidence studies will be followed by case–control studies to obtain detailed data on exposure factors.

Project Dates:
January 1976–continuing.

Financial Support:
DOE, Office of Health and Environmental Research.

1188. NEW MEXICO INSTITUTE OF MINING AND TECHNOLOGY, Department of Psychology, %Socorro, New Mexico 87801.

Project Title:
Flavor Aversion Acquisition Based on Nicotine.

Principal Investigator:
Etscorn, F.T.

Objective:
To study various routes and doses of nicotine capable of producing flavor aversions in rodents.
Methods or Approach:
Using a flavor aversion technique, rats, mice, or hamsters were allowed to drink novel fluids. Following a delay, animals were administered nicotine (i.p. or percutaneous). Single bottle or choice tests were used to determine the degree of aversion.
Results to Date:
Dose-dependent flavor aversions have been demonstrated in rats using cutaneous, but not i.p., routes of nicotine administration. Hamsters showed aversions with i.p. nicotine, but to date the cutaneous route has been unsuccessful.
Future Plans:
The cutaneous route of nicotine administration for aversion acquisition in hamsters will be studied, and bioassays used to determine blood levels of nicotine achieved with the various routes of administration. Tolerance and dependence based on cutaneous delivery will also be investigated.
Project Dates:
July 1980–continuing.
Financial Support:
New Mexico Institute of Mining and Technology.

1189. UNIVERSITY OF NEW MEXICO, NEW MEXICO TUMOR REGISTRY, Cancer Research and Treatment Center, 900 Camino de Salud, NE., Albuquerque, New Mexico 87110.

Project Title:
Uranium Epidemiology Study.

Principal Investigators:
Samet, J.M.; Morgan, M.V.; Key, C.R., et al.
Objective:
To investigate health effects of radon daughter exposures, with emphasis on lung cancer.
Methods or Approach:
A cohort study of mortality of Grants, New Mexico, uranium miners is in progress. A group of approximately 3,000 miners with at least 1 year of underground experience before 1971 has been identified. An additional cohort of miners employed after 1970 will also be established. Radon daughter exposure information is available from State and company sources; cigarette smoking histories have been recorded as part of routine medical evaluations. A retrospective evaluation of the earlier group's mortality through December 31, 1978, is in progress.
Results to Date:
Definitive results from the retrospective cohort study of men first employed before 1971 are not yet available.
Future Plans:
The cohort of miners first employed after 1970 will be expanded, exposure indices will be refined, and followup will be completed.
Project Dates:
December 1977–continuing.
Financial Support:
University of New Mexico; NHLBI (1K04 HL00951); Uranium Industry; DOE

1190. UNIVERSITY OF NEW MEXICO, Department of Medicine, ℅Albuquerque, New Mexico 87131.

Project Title:
Prevalence Survey of Respiratory Disease in New Mexico Hispanics.

Principal Investigator:
Samet, J.M.
Objective:
To conduct a prevalence survey of residents of Belen, New Mexico; characterize epidemiology of respiratory diseases among Hispanics.
Methods or Approach:
In New Mexico, Hispanic male mortality rates for lung cancer and chronic obstructive pulmonary disease are markedly lower than rates for non-Hispanic whites; for females, overall rates are similar, but patterns of age-specific rates differ. Differences in cigarette smoking practices have been suggested as a partial explanation of the differences. The community under study has a stable Hispanic population of approximately 3,900. In a preliminary census, all Hispanic residents will be identified, and it is anticipated that approximately 2,700 children and adults will participate in the investigation. Survey procedures will include completion of standard respiratory symptoms questionnaires, a household questionnaire directed at environmental exposures, and validation of ethnicity, spirometry, and measurement of end-tidal carbon monoxide and salivary cotinine. Analyses will be directed at describing the prevalence of respiratory symptoms and diseases in Hispanics; determining risk factors for respiratory disease; and developing prediction equations for spirometric parameters. The household-based design will also permit assessment of familial aggregation of respiratory diseases and of lung function level. The comprehensive cigarette smoking history obtained will allow comparison of the effects of various types.
Results to Date:
Results are not yet available.
Financial Support:
NHLBI (5R01HL28120-02).

1191. UNIVERSITY OF NEW MEXICO, CANCER RESEARCH AND TREATMENT CENTER, Albuquerque, New Mexico 87131.

Project Title:
Lung Cancer Etiology in Hispanics and Anglos.

Principal Investigator:
Samet, J.M.
Objective:
To explain known differences in lung cancer occurrence between Hispanics and white populations by assessing lung cancer risk factors.
Methods or Approach:
In New Mexico, lung cancer incidence and mortality rates are markedly different in the Hispanic and non-Hispanic white populations; among males, Hispanics have lower rates at all ages, with an overall incidence approximately one-third that of whites. Among females, the overall rates are similar, but Hispanics have lower rates at younger ages and higher rates at older ages. The population-based study of lung cancer risk factors is emphasizing cigarette smoking by type, occupation, passive exposures, and dietary vitamin A. Results of a review of the histopathology of 1980-1983 cases and of 1970-1972 cases will be used to conduct histology-specific analyses.
Results to Date:
By November 1, 1984, interviews had been completed with 600 cases and 787 controls. An additional 50 interviews with 1984 cases are anticipated. Plans for analysis and related computer programming are nearly complete. Completed analyses have examined multiple risk factors for lung cancer, including diet, intake of retinol and carotene, tobacco smoking, residence history, and occupation. The histopathology review has been

completed for the 1970-1972 and the 1980-1981 cases. The investigation will provide new information concerning the epidemiology of lung cancer in Hispanics.

Future Plans:
Established and putative risk factors will be examined in a population-based study.
Financial Support:
NCI (2R01CA27187-04).

New York

1192. ALBERT EINSTEIN COLLEGE OF MEDICINE, 1410 Pelham Parkway South, Bronx, New York 10461.

Project Title:
Child Development to Age Ten and Parental Smoking (British Children).

Principal Investigator:
Rush, D.
Objective:
To assess relationship of prenatal and postnatal parental smoking to child's development and health at age 10.
Methods or Approach:
Longitudinal data have been collected for all children born in Great Britain from April 5 to 11, 1970, who were surveyed at birth and at 5 and 10 years of age. Longitudinal data will be used to relate changing parental smoking to changing child health and development and to control for changed social circumstances. Since much of the effect of smoking in general, and of parental smoking in particular, appears to be contingent on low social status, such effects will be explored. Developmental indices assessed include somatic development, cognition and school achievement, motor coordination, hyperactivity and other behavioral abnormalities, and respiratory illness and symptomatology (reported by both parent and child). Maternal alcohol use during pregnancy will be added as an independent variable as will child's own smoking at age 10 (as a dependent variable and as a determinant of current health and development).
Results to Date:
It has been demonstrated that differences in development between children of smoking and nonsmoking parents at 5 years of age depend in large part on different social and behavioral characteristics of smokers and nonsmokers, although significant, but relatively small, associations do remain after controlling for social and other family differences. Without the extensive social and environmental assessment, analyses would be incomplete, and indeed, misleading.
Financial Support:
NICHD (2R01HD18198-02).

1193. AMERICAN CANCER SOCIETY, 90 Park Avenue, New York, New York 10016.

Project Title:
Evaluation of a Stress-Management Self-Help Guide and Telephone Assistance as Smoking Cessation Methods.

Principal Investigator:
Burton, D.
Objective:
To assess effectiveness of a self-help guide on stress management for the new ex-smoker in increasing maintenance of nonsmoking; assess effectiveness of telephone assistance by an ex-smoker in increasing maintenance of nonsmoking.
Methods or Approach:
The project is being conducted in eight states and includes seven study groups with a total of 2,800 smokers. Groups are (1) usual (self-help cessation pamphlet); (2) stress-management guide; (3) pamphlet plus guide; (4) phone assistance; (5) pamphlet plus phone assistance; (6) guide plus phone assistance; and (7) combined (pamphlet, guide, and phone assistance). Self-reported smoking status will be obtained 1 month and 13 months after initial contact.
Results to Date:
Project is in a preliminary phase.
Project Dates:
February 1985–July 1986.
Financial Support:
ACS.

1194. AMERICAN CANCER SOCIETY, 90 Park Avenue, New York, New York 10016.

Project Title:
FreshStart Group Evaluation.

Principal Investigator:
Burton, D.
Objective:
To assess the effectiveness of the FreshStart group program in yielding cessation for at least 1 year.
Methods or Approach:
Pre- and post-program questionnaires were administered to 1,238 participants in the FreshStart group program. The sample was pooled from eight States. All FreshStart groups were conducted by the American Cancer Society (volunteers or staff). The program consists of four 1-hour sessions; groups average 12 participants. Focus is on stopping quickly and planning strategies for dealing with weight control and stress management. Data on smoking status at 1 year are being collected by an independent research agency. Methodology complies with NIOSH Guidelines for Research on the Effectiveness of Smoking Cessation Programs.
Results to Date:
Results are not yet available.
Future Plans:
A self-help version of FreshStart will be developed and tested.
Project Dates:
March 1984–August 1985.
Financial Support:
ACS.

1195. AMERICAN CANCER SOCIETY, INC. 4 West 35th Street, New York, New York 10001.

Project Title:
Cancer Prevention Study II.

Principal Investigator:
Garfinkel, L.

Objective:
To (1) assess the role of environmental factors in the etiology of various types of cancer; (2) identify those factors which increase the probability of cancer as well as those that have little or no impact on cancer development; (3) analyze the nearly 500 pieces of information initially collected from each person in the study; (4) follow these people for at least 6 years to determine their vital status to better identify cancer causes; and (5) design and promote more effective educational measures for preventing or reducing the impact of identified causes.

Methods or Approach:
The prospective study will collect retrospective data from a large group of Americans (more than 1,000,000) from all walks of life. Confidential questionnaires will be distributed to families which include at least one person 45 years old or older. All persons at least 30 years old in such families are eligible to complete the 4-page questionnaire, which is returned in a sealed envelope. Followup data will be collected every other year for at least 6 years and will include a report of whether the subject is alive or dead. If the participant has died, copies of death certificates will be obtained from State health departments. Mortality analyses will be made when a sufficient number of deaths have been recorded.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Followup periods may be extended after the first 6 years and additional information about certain characteristics or habits may also be collected at various followup times.

Project Dates:
September 1982–1989.

1196. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Formation of Carcinogens During Chewing of Tobacco Mixtures.

Principal Investigators:
Hoffmann, D.; Wenke, G.; Prokopczyk, B.

Objective:
To identify the carcinogenic constituents in betel quid and "paan" (mixtures); devise methods for their reduction and/or inhibition of formation during chewing.

Methods or Approach:
Knowledge on the formation of tobacco-specific N-nitrosamines from tobacco alkaloids has guided model studies for the synthesis of N-nitrosamines derived from areca alkaloids. Analytical studies for the detection of Areca-derived nitrosamines in saliva of chewers utilize GC-TEA techniques. The carcinogenic potential of areca-derived nitrosamines is being assessed in F344 rats.

Results to Date:
Under mild conditions, at least three nitrosamines are formed by nitrosation of arecoline, the major areca nut alkaloid: 3-(methylnitrosamino)propionitrile (MNPN), 3-(methylnitrosamino)propionaldehyde (MNPA), and nitrosoguvacoline (NG). MNPN is a strong carcinogen in F344 rats, causing tumors of the esophagus, tongue, and nasal cavity. MNPA and NG are not or are only weakly carcinogenic in Fischer rats. NG, obtained by nitrosation of areca alkaloids, is found in the saliva of betel quid chewers. The chemistry involved in the nitrosation of arecoline parallels the known chemistry of nicotine; the originally formed 5-(methylnitrosamino)-2-carbomethoxy-2-pentenal reacts further, yielding MNPN and MNPA.

Future Plans:
The question of possible formation of MNPN and MNPA during chewing or on ingestion of precursors will be further elucidated. The in vitro and in vivo metabolism of MNPN and other areca-derived nitrosamines will be studied, providing the basis for elucidation of their role in betel quid carcinogenesis. A possible syncarcinogenic effect of tobacco-specific and areca-derived nitrosamines will also be investigated.

Project Dates:
June 1984–May 1987.

Financial Support:
NCI (2PO129580).

1197. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
N-Nitrosodiethanolamine in Tobacco Carcinogenesis.

Principal Investigators:
Hoffmann, D.; Brunnemann, K.D.

Objective:
To monitor the decline of N-nitrosodiethanolamine (NDELA) levels in currently marketed tobacco products.

Methods or Approach:
Formation of NDELA has been traced to the usage of the sucker growth inhibitor maleic hydrazide-diethanolamine. Federal regulations have prohibited the use of this agent since October 1981. The current project follows the investigation on formation, occurrence, and carcinogenicity of NDELA. Extracts of tobacco or the trapped smoke particulates of tobacco products are chromatographed on silica gel. NDELA-containing fractions are concentrated, sylilated, and analyzed with a modified GC-TEA system.

Results to Date:
Since 1981, NDELA levels in representative commercial cigarettes in the United States have declined by 14 to 32 percent. Levels in snuff tobacco declined by 56 percent, and in chewing tobacco by 33 percent. Present levels of NDELA in tobacco products are still fairly high (in the ppb range).

Future Plans:
Monitoring of representative products will continue through 1987.

Project Dates:
June 1984–May 1987.

Financial Support:
NCI (1-PO1-CA 29580).

1198. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Tobacco Flavor Compounds: Analysis, Mutagenicity and Carcinogenicity.

Principal Investigators:
Hoffmann, D.; LaVoie, E.J.

Objective:
To monitor the chemical composition and genotoxic potential of the smoke of low-tar, low-nicotine cigarettes that are suspected of containing additives; provide assurance that the reduction of toxic and tumorigenic effects of the smoke of low-tar cigarettes is not offset by the presence of flavor components or additives in cigarettes with low tar yields.

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Methods or Approach:
The presence of additives will be monitored by analyzing the essential oils of various commercially available tobacco blends of low-tar cigarettes. The mutagenic potency and chemical composition of tocacco tars obtained from adulterated tobacco from low-tar cigarettes will be compared with tar from 1R1 research cigarettes. Essential oils of the tobacco blends will be obtained by steam-distilling approximately 50 g of tobacco after addition of 150 mL of 0.5N H_2SO_4 until approximately 1 L of distillate is obtained. The chilled distillate will then be extracted three times with 250 mL of CH_2Cl_2. The methylene chloride extract will be dried in vacuo to 30 mL at 20 mm Hg pressure and at 25° C. A capillary GC profile of components will be obtained with a 50-m OV-101 fused silica column programmed from 60° C to 230° C at 2°/minute using a flame ionization detector. Suitability of other capillary GC columns for providing profiles of these essential oils of various tobaccos will also be evaluated.

Results to Date:
Elevated levels of furfural, furfuryl alcohol, 5-methylfurfural, and benzaldehyde were found in several commercial blends of tobacco from low-yield cigarettes compared with tobacco from the 1R1 research cigarette. Anethole and piperonal were also detected as compounds unique to specific commercial tobacco blends.

Future Plans:
Studies will be expanded to include analysis of the steam distillate of the total smoke particulates of various brands of cigarettes.

Project Dates:
June 1981–June 1987.

Financial Support:
NCI (2POCA29580).

1199. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE FOR DISEASE PREVENTION, 1 Dana Road, Vahalla, New York 10595.

Project Title:
Tobacco-Specific Nitrosamine - RIA for DNA Adducts.

Principal Investigator:
Castonguay, A.

Objective:
To develop immunological methods that would facilitate the correlation of the levels and persistence of N'-nitrosonornicotine (NNN) or 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)-DNA adducts with the susceptibility of animal tissues to develop tumors when exposed to NNN or NNK; assess the levels of DNA alkylation in human tissues exposed to tobacco products.

Methods or Approach:
NNN and NNK, which have been isolated from chewing tobacco and from mainstream cigarette smoke, are carcinogenic in strain A mice, F344 rats, and Syrian golden hamsters. Antibodies specific for O^6-methyl-2'-deoxyguanosine (O^6-MedGuo) were produced in rabbits and purified by affinity chromatography. An enzyme-linked immunosorbent assay (ELISA), using biotin-labeled anti-rabbit IgG and avidin-labeled horseradish peroxidase, was developed. BALB mice were immunized with (1) DNA modified with NNN and complexed with methylated bovine serum albumin (MBSA), (2) DNA modified with NNK and complexed with MBSA, and (3) O^4-methylthymidine riboside conjugated to keyhole limpet hemocyanin. Spleen cells will be fused to mouse myeloma cells, and hybridomas producing specific antibodies will be selected.

Results to Date:
Fifty percent inhibition of antibody binding to immobilized O^6-MedGvo-bovine serum albumin was achieved with 2.5 picomoles of O^6-MedGuo. Unmodified nucleosides or 7-methyl-2'-deoxyguanosine were at least 10,000-fold less efficient than O^6-MedGuo in inhibiting the antigen-antibody reaction. Separation of O^6-MedGuo from unmodified nucleosides by high performance liquid chromatography prior to immunoassay allowed detection of 700 femtomoles of O^6-MedGuo in 1 mg of DNA. Four hours after a single i.v. injection of the tobacco-specific carcinogen NNK to F344 rats, O^6-MedGuo was detected in the target tissues: nasal mucosa, lung, and liver; 219, 13.2, and 34.5 micromole O^6-MedGuo/mole dGuo, respectively, but was not detectable in nontarget tissues. Results suggest that methylation at the O^6-guanine site could be important in NNK-mediated carcinogenesis in F344 rats. Data also indicate that ELISA is a very sensitive analytical method that could be used to assess DNA damaged by methylating agents.

Future Plans:
Plans include development of high performance liquid chromatography-BA-ELISA for 7-methylguanine, O^4-methylthymidine, and other tobacco-specific DNA adducts.

Project Dates:
July 1982–June 1985.

Financial Support:
NCI (5RO1CA32391-03).

1200. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Pharmacokinetics of Tobacco-Specific Nitrosamines (TSNA).

Principal Investigators:
Adams, J.D.; LaVoie, F.J.; Hoffmann, D.

Objective:
To determine biological half-lives of tobacco-specific nitrosamines (TSNA) in various species of laboratory animals; study possible correlation with carcinogenic potency.

Methods or Approach:
Extraction of nitrosamines from animal tissues and elution through a Clin-Elut column with ethyl acetate is followed by concentration and analysis by GC-TEA methods.

Results to Date:
Biological half-lives for nitrosonornicotine (NNN), nitrosoanatabine (NAT), 4-(methylnitrosamino)-1-(3-pryidyl)-1-butanone (NNK) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNA1) in F344 rats were 184 and 540 minutes (NNN and NAT), 25 to 37 minutes (NNK), and 184 to 288 minutes (NNA1). A relatively short biological half-life for TSNA suggests correlation with carcinogenic potency.

Future Plans:
Comparative studies on pharmacokinetics of TSNA in various tissues and species will be conducted to determine whether organo-specific carcinogenicity and carcinogenic potency are correlated with short half-life.

Project Dates:
June 1983–continuing.

Financial Support:
Naylor Dana Institute, American Health Foundation; National Cancer Institute (2PO1CA29580).

1201. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Screening for Inhibitors of N-Nitrosamine Carcinogenesis.

Principal Investigator:
Chung, F.-L.
Objective:
To screen for potential dietary-related inhibitors against the tumorigenic effects of nitrosamines by (1) in vitro metabolism; (2) in vivo metabolism and/or DNA adduct formation; and (3) induction of DNA repair.
Methods or Approach:
Fischer rats were pretreated with potential dietary inhibitors and hepatic microsomes were used for metabolism of N-nitrosopyrrolidine (NPYR), dimethyl nitrosamine (NDMN), and 4-(methyl-nitrosamino)-1-(3-pyridyl)-1-butanone (NNK). Esophagus organ culture was used for N′-nitrosonornicotine (NNN) metabolism. For in vivo adduct assay, rats were treated with NDMN and NNK, 4 hours before sacrifice, and hepatic DNA was isolated. Formation of 7 mg and O^6 mg in the DNA samples were measured by high performance liquid chromatography-fluorescence method.
Results to Date:
In the past, 21 dietary and related compounds have been evaluated for potential inhibitory activities against the carcinogenic effects of the structurally related environmental nitrosamines NNN, NPYR, NDMN, and NNK using in vitro metabolism assays. The in vitro metabolism assays were performed in target tissues; rat liver microsomes for NPYR, NDMN, and NNK and cultured rat esophagus for NNN. Among compounds tested (including phenols, cinnamic acids, isothiocyanates, coumarins, indoles) isothiocyanates have been shown to be the most effective inhibitors. The isothiocyanates and the corresponding glucosinolate have been subsequently assayed in in vivo metabolism and/or DNA adduct formation and showed parallel inhibitory activities as in the in vitro assay. Results will allow selection of the most promising inhibitors for further bioassays for the study of the inhibitory activity against tumorigenic effects of nitrosamines. The bioassays are necessary to validate effectiveness of the screening system.
Project Dates:
August 1982–July 1985.
Financial Support:
NCI (2R23CA32272-03).

1202. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Aromatic Amines: Formation During Smoking and Metabolism.

Principal Investigators:
El-Bayoumy, K.; Hoffmann, D.
Objective:
To determine the effect of tobacco nitrate on aromatic amines and nitroaromatics in cigarette smoke; determine effect of smoke inhalation of the metabolism of aromatic amines.
Methods or Approach:
Research will consist of (1) synthesis of (^{14}C)1-nitronaphthalene, (^{14}C)1-nitropyrene, and (^{14}C)6-nitrochrysene as tracers and internal standards; (2) collection of cigarette smoke condensate; (3) solvent partitions and column chromatography; and (4) analysis of the appropriate fraction by gas chromatography with electron capture detection and by combined gas chromatography-mass spectrometry (GC-MS
Results to Date:
The detection limit in GC-MS analysis was approximately 1 μg/injection. From this figure, the number of cigarettes smoked, and recovery of internal standard, it can be estimated that the concentration of 1-nitronaphthalene and 1-nitropyrene did not exceed 10 ng/cigarette and 6-nitrochrysene did not exceed 1 ng/cigarette.
Project Dates:
June 1984–May 1987.
Financial Support:
NCI (P01CA29580).

1203. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road Valhalla, New York 10595.

Project Title:
Tobacco Smoke Components and Atherosclerosis.

Principal Investigators:
Haley, N.J.; Hoffmann, D.
Objective:
To identify and investigate constituents of tobacco smoke that might exert atherogenic effects on the arterial wall.
Methods or Approach:
Syrian golden hamsters are exposed for 18 months to diluted cigarette smoke (gas phase or carbon monoxide at subacute toxicity levels). Additional animals are treated with nicotine or a combination of nicotine and carbon monoxide in proportions consistent with amounts in whole smoke. At necropsy, large arteries will be prepared for histological and biochemical evaluation. Arteries from control and sham-treated animals will be compared with arteries from animals exposed to tobacco smoke.
Results to Date:
Bioassays have been started and animals have slowly acclimatized to increasing exposure levels of tobacco smoke.
Future Plans:
In addition to the mechanisms of action of cigarette smoke constituents on the atherogenic process, the potentiating effects of synergistic risks such as hypercholesterolemia will be investigated.
Project Dates:
April 1984–March 1987.
Financial Support:
NHLBI (1R01HL32204-01).

1204. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Cocarcinogenicity of Ethanol With Nitrosamines.

Principal Investigator:
Hecht, S.S.
Objective:
To investigate the mechanism by which ethanol acts as a cocarcinogen in nitrosamine carcinogenesis.
Methods or Approach:
Nitrosamines to be studied are N-nitrosodimethylamine, N-nitrosodiethylamine, N-nitrosopyrrolidine, N′-nitrosonornicotine, and 4-(methylnitosamino)-1-(3-pyridyl)-1-butanone, constituents in tobacco smoke. In certain cases, carcinogenic activities are known to be increased by chronic ethanol consumption. It is hypothesized that, depending on the

structure of the nitrosamine and target organ, chronic ethanol pretreament can increase rates of metabolic activation by enzyme induction, but that simultaneous exposure to ethanol and the nitrosamine can inhibit nitrosamine metabolism. If the net result is increased metabolic activation, increased carcinogenicity can be expected. To test the hypothesis, rates of metabolic activation of selected nitrosamines will be determined in target organ or cell cultures from ethanol pretreated or control animals. Effects on nitrosamine metabolism of in vitro addition of ethanol will also be determined. When increases in nitrosamine activation are indicated, the extent of formation of carcinogen-DNA adducts in target organs of ethanol pretreated or control animals will be investigated. On the basis of results, the effects of chronic ethanol consumption on the carcinogenicity of selected nitrosamines will be determined.

Results to Date:
Chronic alcohol consumption caused an increase in nasal cavity tumors but a decrease in esophageal tumors in rats treated with N′-nitrosonornicotine, administered in liquid diet containing ethanol. Chronic alcohol consumption increased the rate of metabolic activation of N′-nitrosonornicotine in nasal mucosa of rats, but had no effect in esophageal or lingual mucosa.

Project Dates:
September 1982--continuing.

Financial Support:
NCI (CA 33285).

1205. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Metabolism of the Carcinogen Nitrosonornicotine.

Principal Investigator:
Hecht, S.S.

Objective:
To elucidate the mechanisms by which carcinogenic tobacco-alkaloid-derived nitrosamines are metabolized to intermediates that damage DNA and initiate the carcinogenic process.

Methods or Approach:
Studies will focus on N′-nitrosonornicotine (NNN), 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), 4-(methylnitrosamino)-1-(3-pyridyl)-butanol (NNA1), and N′-nitrosoanatabine (NAT). Human exposure to these carcinogens exceeds that of any other nitrosamine in nonoccupational environments. Previous studies have shown that metabolic alpha-hydroxylation is an important activation process for NNN and NNK. The proposed experiments are designed to confirm the role of alpha-hydroxylation in activation of NNN and NNK and to elucidate the metabolic activation and detoxification pathways of NNA1. Target tissue DNA adducts formed from NNN and NNK will be identified. To accomplish this, products obtained upon reaction of deoxyribonucleosides with diazohydroxides formed in metabolism of NNN and NNK will be structurally characterized and used as markers for identification of DNA adducts formed in vivo upon treatment of rats with high specific activity ^{3}H- or ^{14}C-labeled NNN or NNK. DNA methylation by NNK will be measured by high performance liquid chromatography with fluorescence detection.

Results to Date:
Model compounds for alpha-hydroxylation of NNK, 4-(carbethoxynitrosamino)-1-(3-pyridyl)-1-butanone, and 4-(carbethoxynitrosamino)-4-(3-pyridyl)-1-butanal have been synthesized and allowed to react with deoxyribonucleosides and DNA. The resulting markers are being compared with NNN-DNA adducts formed in rat liver and nasal cavity. NNK has been shown to be more carcinogenic than dimethylnitrosamine, particularly in rat lung. The kinetics of methylation of DNA by the two nitrosamines are being compared.

Project Dates:
April 1977–continuing.

Financial Support:
NCI (CA 21393).

1206. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Carcinogenesis of Tobacco Specific Nitrosamines.

Principal Investigators:
Hecht, S.S.; Hoffmann, D.

Objective:
To better define the relationship between 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) exposure and tobacco-related cancer.

Methods or Approach:
Extensive studies on the formation, occurrence, carcinogenicity, and metabolic activation of tobacco-specific, nicotine-derived nitrosamines support the hypothesis that NNK is a major factor in the causation of tobacco-related cancer. Sensitive methods will be developed to measure levels of the major NNK metabolite 4-(methylnitrosamino)-1-(3-pyridyl)butan-1-ol and levels of NNK-hemoglobin adducts in blood from smokers and chewers. A bioassay of NNK, administered chronically to F344 rats (in drinking water at concentrations of 5 ppm, 1 ppm, and 0.5 ppm), will be carried out.

Results to Date:
Results are not yet available.

Project Dates:
June 1981–continuing.

Financial Support:
NCI (CA 29580).

1207. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Experimental Tobacco Carcinogenesis. A Program Project.

Principal Investigator:
Hoffmann, D.

Objective:
To conduct an interdisciplinary project to (1) elucidate the nature and role of carcinogens in tobacco and tobacco smoke with chemical-analytical methods, bioassays, and biochemical investigations; (2) study the mechanisms of carcinogenesis with model compounds of tobacco-specifc carcinogens and with Areca-derived nitrosamines (which may play a role in the etiology of oral cancer in Asian countries); (3) study aromatic amines with reference to their role in tobacco carcinogenesis; (4) address the question of risk assessment from passive smoke exposure with dosimetry of uptake of environmental smoke pollutants in inhalation bioassays and in human field studies.

Methods or Approach:
The following projects are included in the ongoing program: (1) carcinogenesis of tobacco-specific N-nitrosamines; (2) analytical studies in tobacco carcinogenesis; (3) formation of carcinogens during chewing of tobacco mixtures; (4) formation

of aromatic amines during smoking and metabolism; (5) tobacco flavor compounds; and (6) sidestream smoke carcinogenicity.

Results to Date:
Results are described under individual program projects.

Project Dates.
September 1983–August 1986.

Financial Support:
NCI (CA 35607).

1208. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Endogenous Formation of Nicotine-Derived N-Nitrosamines.

Principal Investigators:
Hoffmann, D.; Castonguay, A.

Objective:
To (1) quantitate the documented nitrosation potential of inhaled cigarette smoke by utilizing GC-TEA methods and radioimmunoassays for N-nitrosoproline (NPRO), a stable urinary excretion product resulting from endogenous nitrosation of L-proline; (2) correlate NPRO formation with that of nicotine-derived nitrosamines; and (3) examine whether 5-(3-pyridyl)proline, given to mice, rats, and hamsters, is converted to N-nitroso-5-(3-pyridyl)proline when animals are exposed to cigarette smoke in inhalation studies.

Methods or Approach:
N-nitroso-5-(3-pyridyl)proline, if formed endogenously, would serve as an appropriate indicator for the degree of endogenous nitrosation of carcinogenic nicotine-derived nitrosamines. Urine specimens of snuff users, cigarette smokers, nonsmokers, and nonsmokers exposed to environmental tobacco smoke (all on a controlled diet) will be analyzed by GC-TEA methods and radioimmunoassays for nicotine, cotinine, and N-nitrosoproline (NPRO). N-nitroso-5-(3-pyridyl)proline and 5-(3-pyridyl)proline will be synthesized as an exposure marker and as model compounds for bioassays, respectively. The nitrosation potential of cigarette smoke will be comparatively assessed in humans and in studies with hamsters. Ultimately, the studies should lead to measures for the inhibition of in vivo formation of such carcinogens.

Results to Date:
Syntheses of model compounds are in progress and radioimmunoassays for NPRO are being developed. After enrichment by extraction procedures and GC-TEA determination of urinary N-nitrosoproline, it was seen that significant endogenous nitrosation occurs in cigarette smokers and snuff-dippers, while there was no measurable nitrosation potential for environmental smoke under experimental conditions employed.

Project Dates:
September 1983–August 1986.

Financial Support:
NCI (CA 35607).

1209. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Experimental Tobacco Carcinogenesis: Sidestream Smoke Carcinogenicity.

Principal Investigators:
Hoffmann, D.; Haley, N.J.

Objective:
To investigate the carcinogenic potential of sidestream smoke inhalation in laboratory animals; evaluate absorption of sidestream smoke constituents by human subjects under controlled and field conditions.

Methods or Approach:
Syrian golden hamsters will be exposed daily to the maximum tolerated dose of sidestream or mainstream smoke generated by a Hamburg II smoking machine for a period of 24 months. Results at necropsy will be compared with those of control and sham-treated animals. Clinical studies will evaluate absorption of nicotine and other tobacco smoke constituents by volunteers who will be monitored in a specially constructed room and in free-living situations.

Results to Date:
Animals are being treated to establish the maximum tolerated dose of smoke pollutants, and inhalation bioassays are being set up based on findings. Humans exposed to sidestream smoke pollutants generated by two, three, or four cigarettes (smoked continuously over an 80 min period) in a controlled environment absorb and excrete nicotine and also detoxify it to cotinine in a dose-related fashion.

Project Dates:
June 1984–May 1987.

Financial Support:
NCI (2P01CA2950).

1210. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Experimental Tobacco Carcinogenesis: Tobacco Smoke and Bladder Carcinogenesis.

Principal Investigators:
Hoffmann, D.; Lavoie, E.J.

Objective:
To evaluate effects of cotinine and nicotine-N′-oxides on development of tumors in rats initiated with N-(4-(4-nitro-2-furyl)-thiazolyl)-formamide (FANFT); determine effects of catechol administration on urinary bladder of rats treated with N-butyl-N-(4-hydroxybutyl)nitrosamine.

Methods or Approach:
When Fischer rats were 6 weeks old, FANFT was administered in an agar diet for a 6-week period. Subsequently, cotinine (0.1 percent), trans-nicotine-N′-oxide (0.02 percent), and a mixture of cis- and trans-nicotine-N′-oxide (0.02 percent), given as promoters, were offered ad libitum for 78 weeks. Control groups consisted of rats receiving tap water with/without prior administration of FANFT. The effect of catechol on development of urinary bladder tumors was studied in rats treated with N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN). A solution of 0.05 percent catechol and 0.001 percent BBN was administered in drinking water ad libitum for 78 weeks. Urinary bladders were removed and examined microscopically.

Results to Date:
Cotinine, trans-nicotine-N′-oxide, and the mixture of cis- and trans-nicotine-N′-oxide were not carcinogenic and did not promote urinary bladder tumors initiated with FANFT in rats. Tumor formation in the tongue and palate observed in FANFT-treated rats was not affected by administration of the nicotine metabolites. There was, however, a significant increase in incidence of tumors of the forestomach in rats initiated with FANFT, who subsequently received either trans-nicotine-N′-oxide or a mixture of cis- and trans-nicotine-N′-oxide. Animals

receiving 0.05 percent catechol alone in drinking water had neither macroscopically nor microscopically detectable lesions significantly different from those in control animals that had received tap water. Urine analyses of animals receiving catechol indicated that >99 percent of catechol present was as either glucuronide or sulfate conjugates. No statistically significant difference was observed between the experimental group receiving 0.001 percent BBN with 0.05 percent catechol and animals receiving 0.001 percent BBN alone with respect to incidence of hyperplasia, papilloma, or carcinoma of the urinary bladder.

Future Plans:

The effects of nicotine-N′-oxides on thyroid hormone levels and on tumorigenicity in mice will be investigated.

Project Dates:

June 1981–May 1984.

Financial Support:

NCI (CA 29580).

1211. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:

Experimental Tobacco Carcinogenesis: Analytical Studies in Tobacco Carcinogenesis.

Principal Investigators:

Hoffmann, D.; Brunnemann, K.D.

Objective:

To develop highly sensitive methods for detection of amides and their N-nitrosoanalogues in tobacco, in tobacco smoke, and in saliva of tobacco users.

Methods or Approach:

Analytical studies in tobacco carcinogenesis are designed to apply state-of-the-art techniques to assay classes of chemical compounds in tobacco or tobacco smoke that have not been previously assessed because of their high reactivity or low limits of detection. Indirect assessment of nitrosamides in tobacco smoke is being attempted by identifying N-nitroso-N-methylnicotinamide and N-nitroso-N-methylacetamide. Development of the procedure and investigations on all analytical challenges with other compounds are in process using various approaches. Other compounds to be quantified are formaldehyde and other volatile aldehydes, α-ketoaldehydes, volatile carbonyl compounds, and volatile N-nitrosamines in mainstream and sidestream smoke. Analyses of environmental smoke pollutants and their uptake by humans are also conducted.

Results to Date:

Project is in a preliminary phase.

Future Plans:

The scope of analytical challenges may be broadened if time permits.

Project Dates:

June 1984–May 1987.

Financial Support:

NCI (CA 29580).

1212. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Vahalla, New York 10595.

Project Title:

Effects of Catechol on the Metabolism and DNA-Binding of (^3H)Benzo(*a*)pyrene in Mouse Skin In Vivo.

Principal Investigator:

Melikian, A.A.

Objective:

To study the basic mechanism by which catechol enhances the tumorigenic activity of benzo(*a*)pyrene (BaP) in mouse skin.

Methods or Approach:

Catechol is a cocarcinogen with BaP in initiation/promotion assays on mouse skin; both are present in cigarette smoke at levels of 0.04 to 0.28 mg/cigarette and 10 to 50 ng/cigarette, respectively. Effects of catechol on the metabolic activation of (^3H)BaP in mouse skin and on binding of BaP metabolites to DNA and proteins at intervals from 0.5 to 24 hours after treatment were studied. Mice were sacrificed at certain intervals after treatment with 0.015 mg (^3H)BaP and either 0.25 mg or 0.5 mg catechol in 0.15 mL acetone, applied to the shaved back. Treated areas of skin were isolated and metabolites of (^3H)BaP were extracted from the epidermal layer and analyzed for glutathione, glucuronide, and sulfate-conjugated and unconjugated metabolites. Another group of similarly treated mice was used for DNA and protein isolation. Syn- and anti-isomers of trans-7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydro-BaP bound to DNA were quantitated after enzymatic hydrolysis of DNA to deoxyribonucleoside and separation by Sephadex LH-20 and boronate chromatography.

Results to Date:

Catechol did not affect the total amount of (^3H)BaP metabolized in mouse skin; however, it changed the proportion of the various metabolites formed. Catechol increased water soluble (^3H)BaP metabolites, tetraols, and quinones, and doubled levels of unconjugated 3-hydroxy-BaP (0.5 to 24 hours after treatment). It also increased levels of trans-7,8-dihydroxy-7,8-dihydro-BaP, and trans-9,10-dihydroxy-9,10-dihydro-BaP 0.5 to 2 hours after treatment; levels decreased to control levels 2 hours after treatment. Catechol did not affect levels of glutathione conjugates; however, glucuronide and sulfate formation was decreased 0.5 hour after treatment. Catechol increased binding of trans-8,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydro-BaP (BPDE) to DNA 2.3-fold. It also increased the ratio of anti- and syn-isomers of BPDE-DNA and binding to proteins.

Future Plans:

The effects of 3-hydroxy-BaP in the binding to DNA will be investigated.

Project Dates:

December 1983–December 1985.

Financial Support:

NIEHS (ES 03278).

1213. AMERICAN HEALTH FOUNDATION, Division of Health Promotion Research, 320 East 43rd Street, New York, New York 10017.

Project Title:

Smoking Prevention: The Youth Health Promotion Project.

Principal Investigator:

Orlandi, M.A.

Objective:

To evaluate the relative effectiveness of two different approaches to implementing a school-based smoking prevention program.

Methods or Approach:

The first approach introduces smoking prevention as one part of a multiple risk factor intervention; the second approach introduces smoking prevention as a stand-alone program. The approaches are being tested in a longitudinal 5-year field study utilizing random assignment and schools as units of randomization. Students will be followed from grade 6 through grade 10. The project, which is being implemented throughout three school districts in New York City, involves 16 junior high schools with approximately 6,000 students. The primary dependent variable is smoking onset rate as measured by self-report with saliva cotinine validation. Changes in other health behaviors, health knowledge, and health attitudes will also be compared in treatment vs. control groups. An intensive formative evaluation will attempt to identify the process variables related to program success or failure in the two treatment conditions.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Results are expected to provide a framework for a meta-analysis of school-based prevention programs with special emphasis on issues of implementation and diffusion.

Project Dates:
September 1984–August 1989.

Financial Support:
NCI (R01CA38219-01).

1214. AMERICAN HEALTH FOUNDATION, 320 East 43rd Street, New York, New York 10017.

Project Title:
Primary Prevention of Cancer in Childhood; Coronary Risk Factor Intervention in Childhood.

Principal Investigator:
Walter, H.J.

Objective:
To reduce risk for future development of chronic disease through modification of risk factors in schoolchildren; reduce incidence of cigarette smoking and shift population means and distributions of blood pressure, blood lipid levels, body mass indices, and cardiovascular fitness.

Methods or Approach:
The two projects were randomized longitudinal intervention studies conducted in two demographically dissimilar populations: (1) Bronx, New York, approximately 2,000 students (50 percent black, 25 percent white, 25 percent other); and (2) Westchester County, New York, approximately 1,500 students (85 percent white, 15 percent other). In both studies, approximately half of the students were randomly assigned to intervention, the other half serving as controls. Beginning in fourth grade and continuing through the ninth grade, the intervention group received the "Know Your Body" program that focuses on nutrition, physical fitness, and prevention of smoking. In addition to health knowledge, attitudes, and behaviors, outcome measures included weight, triceps skinfold thickness, systolic and diastolic blood pressure, postexercise pulse recovery rate, plasma total and high density lipoprotein cholesterol, and saliva cotinine.

Results to Date:
Preliminary data indicate statistically significant differences between intervention and control groups for knowledge, dietary behaviors, blood pressure, total cholesterol, and cigarette smoking.

Future Plans:
Cohorts will be followed through 12th grade to determine whether favorable outcomes are maintained, increased, or decreased.

Project Dates:
July 1979–June 1985.

Financial Support:
NCI (CA 25521); NHLBI (HL 21891).

1215. AMERICAN HEALTH FOUNDATION, NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Interdisciplinary Studies in Cancer Epidemiology: Biochemical Estimation of Smoking Behavior.

Principal Investigators:
Wynder, E.L.; Haley, N.J.

Objective:
To estimate prevalence and extent of compensation that occurs as smokers switch to low-yield cigarettes; determine importance of nicotine strength of previous cigarettes and current consumption in regard to blood levels of nicotine and cotinine and absorption of gas phase components.

Methods or Approach:
The 2,000 smokers recruited through blood banks in the metropolitan New York area fill out a detailed questionnaire on smoking history and provide a venous blood sample. Carboxyhemoglobin, nicotine, cotinine, and thiocyanate are measured in each sample and correlated with self-reported current cigarette usage and past experience.

Results to Date:
Circulating levels of cotinine in smokers who switched to low-yield cigarettes are generally higher than in smokers who have always smoked low-yield brands. No correlation was found between carbon monoxide, hydrogen cyanide, or nicotine yields and current consumption levels.

Future Plans:
The project will concentrate on heavy smokers and their capacity to metabolize nicotine. Data will be correlated with data on long-term light smokers.

Project Dates:
September 1982–August 1985.

Financial Support:
NCI (5P01CA32617-03).

1216. AMERICAN HEALTH FOUNDATION, 320 East 43rd Street, New York, New York 10017.

Project Title:
Studies in Tobacco-Related Cancers.

Principal Investigators:
Wynder, E.L.; Goodman, M.T.; Kabat, G.C., et al.

Objective:
To (1) measure effect of smoking cigarettes with varying levels of tar and nicotine on risk of developing five selected tobacco-related diseases; (2) monitor use of newer low-tar cigarettes by hospital cases and controls; (3) identify individuals or groups at high risk for tobacco-related diseases; and (4) analyze relative effects of cigarette modification that characterize candidate less-hazardous cigarettes.

Methods or Approach:
Hospital patients who meet study criteria are interviewed in selected hospitals in New York, Philadelphia, Atlanta, Pittsburgh, Chicago, and San Francisco. Cases are persons with a histologically confirmed diagnosis of cancer of the lung, bladder, pancreas, esophagus, or oral cavity, or first myocardial infarction. Controls (patients without tobacco-related disease matched by race, sex, and age) are administered the same structured questionnaire. Approximately 1,260 cases and 2,500 controls will be interviewed each year. Data will consist of descriptive analyses of epidemiologic patterns associated with various levels of exposure to tobacco smoke, particularly use of low-tar cigarettes, and analyses of odds ratios for the different study sites associated with use of low-tar cigarettes and other

hypothesized risk factors. Effects of modifier, extraneous, or nuisance variables will also be evaluated using multiple logistic procedures.

Results to Date:
An investigation of the association between mouthwash use and oral cavity cancer demonstrated an association only in females, after adjusting for smoking and alcohol consumption. However, the association was probably not causal. An analysis of the role of different types of alcoholic beverages (beer, wine, hard liquor) in relation to oral cavity cancer is currently in progress. Analysis of data on a large population of controls, characterizing variables associated with cigarette preference has been published. Currently, analysis of 76 male and 76 female nonsmoking bladder cancer cases and controls is being completed. No association was found for exposure to sidestream smoke, coffee drinking (brewed or decaffeinated), or artificial sweetener use. The association of several occupations with bladder cancer risk has been found in males, although the sample size was small. Preliminary results from analysis of lung cancer cases (squamous and adenocarcinoma) have shown a significant effect of cigarette tar on risk of squamous cell cancer in men, even after controlling for the main effects of duration and average number of cigarettes smoked/day. In general, filter-tipped cigarette smokers appear to be at 20 percent lower risk of squamous cell lung cancer than nonfilter cigarette smokers.

Project Dates:
June 1982–June 1985.

Financial Support:
NCI (P015CA32617).

References:
(1) Wynder, E.L.; Kabat, G.; Rosenberg, S., et al. "Oral Cancer and Mouthwash Use." *Journal of the National Cancer Institute* 70(2):255-260, 1983. (2) Wynder, E.L.; Goodman, M.T.; Hoffmann, D. "Demographic Aspects of the Low-Yield Cigarette: Consideration in the Evaluation of Health Risk." *Journal of the National Cancer Institute* 72(4):817-822, 1984.

1217. AMERICAN LUNG ASSOCIATION OF MID-NEW YORK, INC., 23 South Street, Utica, New York 13501.

Project Title:
Youth Council Against Smoking.

Principal Investigator:
Littlefield, J.

Objective:
To develop a peer teaching program in which high school students teach fourth graders.

Methods or Approach:
The program, which is conducted in cooperation with the local chapters of the American Cancer Society and the American Heart Association, utilizes audiovisual materials developed by the agencies. High school students are trained in a 1-day workshop to teach topics such as disease states and the respiratory system. They also listen as a teacher discusses the emotional, physical, and intellectual levels of fourth grade students. High school students also develop leadership capabilities and skills in areas such as assertiveness, group dynamics, and public speaking.

Results to Date:
The program helps both younger and older students gain knowledge about the health hazards of smoking and to develop a positive self-image.

1218. AMERICAN LUNG ASSOCIATION, 1740 Broadway, New York, New York 10019.

Project Title:
Prospective Evaluation of Abstinence Behavior in the American Lung Association's Freedom From Smoking (FFS) Clinics.

Principal Investigators:
Freedman, B.D.; Kafalas, T.

Objective:
To (1) measure the rates of continuous abstinence (from cigarettes and other tobacco products for 12 months without acknowledged relapse to smoking) and nonsmoking prevalence (abstinence from smoking for the 30-day period prior to 12-month followup) as a consequence of participation in the Freedom From Smoking (FFS) clinic; (2) to establish client profiles of FFS clinic participants; and (3) to provide a management system for tracking success of program objectives.

Methods or Approach:
Client profiles include demographic attributes, smoking characteristics (nicotine self-regulation, daily cigarette consumption, age of smoking onset), and perception of various components of the clinic (e.g., strength of moderator, adequacy of relapse prevention, effectiveness of cessation skills). Questionnaires were administered at program onset, end of treatment, and 12 months later (phone or mail contact). Questionnaires elicit responses primarily by closed-ended format with unaided recall. Smoking status, daily consumption, use of alternative tobacco products, and aspects of nicotine titration are obtained. Participating lung associations forward clinic data sets to the American Lung Association's Epidemiology and Statistics Unit for editing and computer entry. Rates of continuous abstinence, nonsmoking prevalence, and attrition are computed from the 12-month data sets. Persons lost to followup are treated as continuing smokers. All reports follow Guidelines for Group Smoking Cessation Programs, established by the Peer Review Groups of the National Center for Health Education.

Results to Date:
Attendance at FFS clinics at 54 sites in 1983 totaled 1,562 smokers. At end of treatment, data was available for 813 (416 smokers, 397 ex-smokers). At 12 months, data were available for 964 clinic participants. Nonsmoking prevalence at end of treatment was 48.8 percent; at 12 months, 22.40 percent of total participants. Rates for 1983 appear to replicate earlier findings in 1981 and 1982; 95 percent confidence intervals for 1983 show higher upper bounds than those for 1981 and 1982, suggesting that 1983 FFS clinics did better than clinics held during the earlier 2 years.

Future Plans:
The project will be continued as an ongoing activity.

Project Dates:
December 1981–continuing.

Financial Support:
ALA.

1219. AMERICAN LUNG ASSOCIATION, 1740 Broadway, New York, New York 10019.

Project Title:
Primary Grades Health Curriculum Project - Longitudinal Study.

Principal Investigator:
Andrews, R.L.

Objective:
To determine the impact of the Primary Grades Health

Curriculum Project on children's knowledge about health, attitudes toward health, and present and future health practices of participating students and their families.

Methods or Approach:

An experiment using a pretest-posttest and posttest-only control group design was conducted among 516 children who entered kindergarten in three medium-sized suburban school districts in September 1977. Curricular materials and methods for health education through sixth grade were (1) group 1 (experimental group), Primary Grades Health Curriculum Project (PGHCP) in kindergarten through third grade, and the School Health Curriculum Project (SHCP) in grades 4, 5, and 6; (2) control group 1, standard, commonly used methods and curricular materials for health education in kindergarten through third grade and SHCP in grades 4, 5, and 6; and (3) control group 2, standard elementary curriculum materials and methods for health education in kindergarten through sixth grade. To test study hypotheses, 89 variables were identified and analyzed. Precautions were taken to assure validity of study data. Anonymity of parental responses to questionnaires was assured through precoding.

Results to Date:

Results indicate that there were significant differences between the experimental and control groups in affective and cognitive posttests (sixth grade), but no difference in health locus of control. Children in the experimental group evidenced significantly more positive attitudes toward good health practices and more negative attitudes toward smoking than children in either control group. Data provide evidence that the PGHCP and SHCP curricula have a positive impact on children's current levels of knowledge about health and attitudes toward health and have a positive impact on present and future health practices of students and their families. Early intervention with children as they enter school, compared with intervention only during the early onset years or with standard elementary school health curricula, has a positive impact on level of health knowledge and attitudes. Exposure to the PGHCP in conjunction with the SCHP reduces risk of onset of substance abuse by children compared with children who have received only the SHCP or a standard health curriculum. Interaction between early intervention and intervention during the onset years has a more positive impact on health profiles of children than intervention during onset years only.

Future Plans:

The longitudinal study will continue until the test group completes 11th grade. Testing will take place every other year (beginning June 1983).

Project Dates:

November 1975–June 1989.

Financial Support:

ALA.

1220. BEHAVIORAL HEALTH SYSTEMS, 650 Victory Boulevard, Staten Island, New York 10301.

Project Title:

A Computer-Mediated Smoking Cessation Program.

Principal Investigators:

Tooley, J.; Schneider, S.J.

Objective:

To develop a self-help smoking cessation system as part of the EIES computer conferencing center at the New Jersey Institute of Technology.

Methods or Approach:

The system will offer on-line behavioral smoking cessation instruction tailored to individual participants. It will also offer a conference of smokers for mutual support, consultation with conference moderators, and a system for immediate intervention to manage smoking urges. The system will be compared with a similar but noninteractive computerized system. Abstinence rates will be compared, as will relapse rates and the nature of the smoker who benefits from each system.

Results to Date:

Computer systems have been developed and evaluation will begin.

Future Plans:

Systems will be further refined and tested in a larger sample of smokers. Following testing, the system may be made available to the general public.

Project Dates:

October 1984–March 1985.

Financial Support:

NHLBI (HL33053-01).

1221. BROOKHAVEN NATIONAL LABORATORY, MEDICAL RESEARCH CENTER, Upton, New York 11973.

Project Title:

Environmental and Industrial Exposure to Heavy Metals: Dose Response Analysis.

Principal Investigator:

Ellis, K.J.

Objective:

To (1) determine the degree of human exposure to cadmium (Cd), mercury (Hg), and lead (Pb) using in vivo measurement techniques; (2) examine interrelationships between the body burden obtained by these methods and indirect monitoring techniques using blood, urine, and hair samples; and (3) examine possible synergistic effects of other factors such as smoking, diet, and general health.

Methods or Approach:

Direct in vivo assessment of Cd, Hg, and Pb are made using either prompt gamma neutron activation analysis or x ray fluorescence. Kidney and liver burdens of Cd are measured and bone level stores are obtained. Environmental and/or industrial exposure conditions are obtained and extensive biochemical and clinical chemistry tests are performed to quantify an individual's health status. Assays can include β-microglobulin, MT, ZPP, and levels of Cd, Hg, or Pb in urine and blood.

Results to Date:

Excessive exposure to heavy metals results in significant adverse health effects. Renal abnormalities are evident. Body burden levels and distribution would suggest renal abnormalities may not be evident until a number of years after exposure; e.g., redistribution of Cd from the liver to kidney is a gradual process. Effects of cigarette smoking are evident at all levels of exposure. Cigarettes both provide a source of metal exposure and appear to enhance the body burden levels for industrial workers.

1222. CITY UNIVERSITY OF NEW YORK, MOUNT SINAI SCHOOL OF MEDICINE, Fifth Avenue at 100th Street, New York, New York 10029.

Project Title:

Role of the Father in His Daughter's Drug Use.

Principal Investigators:

Brook, J.S.; Brook, D.

Objective:

To examine paternal personality characteristics and childrearing practices as they relate to the daughter's drug use; examine the interaction of paternal factors with adolescent personality attributes and family and peer systems in relation to females' choice of drugs and mild versus heavy use of tobacco and marijuana.

Methods or Approach:

Self-administered questionnaires were given to 403 female college students (from intact homes) and their fathers in 1982. Both the student and the father questionnaires included a number of scales with adequate psychometric properties designed to tap paternal personality characteristics, paternal childrearing practices, adolescent personality attributes and family and context and peer variables. A series of questions on both licit and illicit drug use pertaining to the adolescent as well as to significant others in her environment was included. Data obtained were compared with data in a current father-son study, so that the father's role in his offsprings' development could be more comprehensively assessed. Hierarchical multiple regression was the primary analytic technique. The study provided data on the paternal determinants of female drug use, (an area about which very little is known), greater understanding of the father's role in the family, and a more complete knowledge of drug use; all are necessary for prevention and treatment of adolescent drug use.

Results to Date:

Results of the study, which has been completed, have been published.

Project Dates:

June 1, 1982–June 30, 1984.

Financial Support:

NIDA (5RO1DA02390-03).

References:

(1) Brook, J.S.; Whiteman, M.; Gordon, A.S., et al. "Paternal Determinants of Female Adolescent's Marijuana Use." *Developmental Psychology* 20:1032-1043, 1984. (2) Brook, J.S.; Whiteman, M.; Gordon, A.S., et al. "Father's Influence on His Daughter's Marijuana Use Viewed in a Mother and Peer Context." *Advances in Alcohol and Substance Abuse* (In press).

1223. CITY UNIVERSITY OF NEW YORK, MOUNT SINAI SCHOOL OF MEDICINE, 1 Gustave Levy Place, New York, New York 10029.

Project Title:

Controlled Psychologic Study of Asbestos Exposure.

Principal Investigator:

Lebovits, A.H.

Objective:

To (1) assess the long-term psychological impact of the disclosure of oncogenic exposure, specifically asbestos; (2) assess the subset of the group at risk who, by virtue of continuing to smoke cigarettes, escalate their cancer risk; and (3) investigate the presence of potentially predictive psychological factors among an increased-risk group as a feasibility study preparatory to a longitudinal prospective assessment.

Methods or Approach:

This is a 4-year psychological study of (1) men who were employed in asbestos work 20 to 40 years ago; (2) a comparison group of postal workers without known oncogenic exposure but comparable in age, race, and socioeconomic level; and (3) patients with mesothelioma.

Results to Date:

To date, 130 asbestos workers, 100 postal workers and 250 mesothelioma patients have been evaluated. Asbestos workers did not appear to be more psychologically distressed than the comparison group of non-exposed postal workers, both presently and in the past. Risk information did not appreciably affect health behaviors such as smoking cessation or usage of masks. There were differences, however, between smokers and nonsmokers among asbestos workers that centered on perceptions of control of health and intrusiveness of medical risk status. Mesothelioma patients were a psychologically distressed group, exhibiting a significant level of depression. The lack of observed psychological distress along with nonadaptive behaviors in the exposed disease-free group may indicate that denial is a common coping mechanism to chronic occupational exposures. Asbestos-exposed individuals therefore may have a strong need for intervention in the at risk phase to combat denial and enhance the adaptive use of risk information to support health-promoting behaviors. Intervention is also needed in the illness phase to cope with frequently encountered depressive disorders.

Project Dates:

July 1981–December 1985.

Financial Support:

NIEHS (1RO1ES02578).

1224. COLUMBIA UNIVERSITY, COLLEGE OF PHYSICIANS AND SURGEONS, 630 West 168th Street, New York, New York 10032.

Project Title:

Cigarette Smoking in Normotensive and Hypertensive Subjects: Blood Pressure, Renin, Aldosterone and Catecholamine Responses.

Principal Investigator:

Baer, L.S.

Objective:

To determine the effects of cigarette smoking in normotensive and hypertensive subjects.

Methods or Approach:

Normotensive and hypertensive subjects were studied to determine their blood pressure, renin, aldosterone, and catecholamine responses to cigarette smoking.

Results to Date:

Cigarette smoking in hypertensive patients acutely increases blood pressure, pulse rate, plasma ACTH, aldosterone, cortisol, and catecholamines. Plasma renin activity does not increase after cigarette smoking.

Future Plans:

Studies will be conducted to determine whether nicotine is the agent responsible for the hormonal and blood pressure effects. Methods for reducing the hormonal and hemodynamic effects of cigarette smoking will also be investigated.

Project Dates:

January 1978–December 1985.

Financial Support:

General Clinical Research Center (RR 00645-13).

Reference:

Baer, L. "Cigarette Smoking in Normotensive and Hypertensive Subjects." *American Journal of Medicine* (In press).

1225. COLUMBIA UNIVERSITY, SCHOOL OF PUBLIC HEALTH, 60 Haven Avenue, New York, New York 10032.

Project Title:

Changing Drug Abuse Patterns and Treatment Needs.

Principal Investigator:

Brunswick, A.F.

Objective:

To (1) continue the longitudinal study of health and substance behavior in a representative sample of urban black youth into a third wave at ages 26 to 31; (2) analyze the trajectories of onset and termination in use of all substances, including cigarettes, alcohol, and illicit substances from adolescence on; and (3) construct trajectories of health problems and health status over the 15 years the sample has been followed since adolescence.

Methods or Approach:
Both bivariate and multivariate statistics are applied to data obtained through individual home interviews. Findings are based on gender-specific tests.

Results to Date:
Results from earlier waves concerning influences on smoking initiation and gender differences both in patterns of smoking behavior and their influences have been published.

Project Dates:
September 1982–August 1985.

Financial Support:
NIDA (1R18 DA03287).

References:
(1) Brunswick, A.F.; Messeri, P. "Causal Factors in Onset of Adolescents' Cigarette Smoking: A Prospective Study of Urban Black Youth." In: Shaffer, H.; Stimmel, B. (Editors). *The Addictive Behaviors.* Advances in Alcohol and Substance Abuse Volume 3(1-2) New York, Haworth Press, 1983-1984, pp. 35-52. (2) Brunswick, A.F.; Messeri, P.A. "Gender Differences in the Processes Leading to Cigarette Smoking." *Journal of Psychosocial Oncology* 2(1):49-69, 1984. (3) Brunswick, A.F. "Origins of Cigarette Smoking in Academic Achievement, Stress and Social Expectations." *Journal of Early Adolescence* 4(3), 1984 (In press).

1226. COLUMBIA UNIVERSITY, COLLEGE OF PHYSICIANS AND SURGEONS, 630 West 168th Street, New York, New York 10032.

Project Title:
Cigarette Smoke Impairs Elastin Resynthesis in Lungs of Hamsters With Elastin-Induced Emphysema.

Principal Investigator:
Osman, M.

Objective:
To determine effect of cigarette smoke on elastin repair in experimental emphysema.

Methods or Approach:
After induction of emphysema by intratracheal administration of elastase, hamsters were exposed to cigarette smoke for 1 week, and the following determinations were made: (1) C^{14} lysine incorporation into the crosslinks, desmosine and isodesmosine, as an indicator of the crosslink elastin repair; (2) elastin content, as an indicator of the balance between elastin degradation and repair; (3) mean linear intercept, as an indicator of the severity of emphysema; and (4) lysyl oxidase, as a supporting parameter for measurements of elastin crosslink formation.

Results to Date:
After exposure to cigarette smoke, ^{14}C lysine incorporation into desmosine and isodesmosine and lysyl oxidase activity were inhibited in hamsters.

Future Plans:
Further investigations will be conducted to determine whether elastin repair is due to (1) inability to produce lysyl oxidase; (2) inactivation of lysyl oxidase; (3) a decrease in tropoelastin production; (4) interference between lysyl oxidase and tropoelastin as a substrate; and (5) the effect of long-term exposure of cigarette smoke on elastin repair.

Project Dates:
May 1983–April 1986.

Financial Support:
USPHS (15832).

1227. COLUMBIA UNIVERSITY, SCHOOL OF PUBLIC HEALTH, 60 Haven Avenue, New York, New York 10032.

Project Title:
Molecular Cancer Epidemiology–BaP-DNA Binding.

Principal Investigator:
Weinstein, I.B.

Objective:
To conduct in vivo studies to validate a recently developed immunoassay for benzo(*a*)pyrene covalently bound to DNA as a dosimeter for "biologically effective dose" of the carcinogen; evaluate potential of the assay as an indicator of increased risk of lung cancer.

Methods or Approach:
The study will investigate relatively unknown aspects of in vivo binding, including sensitivity of the assay, dose–response relationships, persistence of the adduct, extent of interindividual variation, correlation between concentrations of adducts in lung and white blood cell DNA in laboratory animals, and the possibility that lung cancer patients have a greater tendency to bind BaP to DNA than controls. Research will consist of (1) experimental studies of limited numbers of laboratory animals and highly exposed cigarette smoking volunteers in which exposure to BaP will be controlled and (2) observational and clinical studies of coke-oven workers and lung cancer cases and controls. DNA extracted from lung and blood samples of animals and blood samples of humans will be assayed by the same enzyme-linked immunosorbent assay (ELISA). For human subjects, results in the ELISA will be analyzed in conjunction with data obtained by questionnaire concerning exposure to BaP and to a limited number of agents believed to modify BaP metabolism in humans. An attempt will be made to verify results of an earlier pilot project involving laboratory animals and hospital patients and develop meaningful data on the potential of the BaP-DNA assay for use as a dosimeter in future molecular epidemiological studies in cancer causation, and as a means of screening individuals who might be at elevated risk of lung cancer.

Results to Date:
Results are not yet available.

Financial Support:
NCI (5R01CA35809-02).

1228. COLUMBIA UNIVERSITY, COLLEGE OF PHYSICIANS AND SURGEONS, Department of Obstetrics and Gynecology, 622 West 168th Street, New York, New York 10032.

Project Title:
Fetal Hypoxia and Maternal Smoking.

Principal Investigators:
James, L.S.; Stark, R.; Fox, H., et al.

Objective:
To provide better methods for detection and assessment of fetal hypoxia; determine ways in which smoking adversely affects the fetus.

Methods or Approach:
The cardiovascular, respiratory, and biochemical responses of the fetus to both hypoxia and smoking will be studied during development. To gain insight into mechanisms involved,

parallel observations will be made in the human fetus and the chronically instrumented subhuman primate in which direct measurements of biochemical and biophysical parameters can be made. The effects of autonomic mediators on electrophysical characteristics of the developing heart will be studied in the presence of hypoxia and acidosis. Structure and composition of the placenta during pregnancy, in association with smoking, will be characterized. The type of growth retardation caused by smoking, the timing of this effect, and the potential for the fetus to recover will be determined.

Results to Date:
Carboxyhemoglobin levels were significantly greater at each visit for smokers compared with nonsmokers ($p < 0.001$), but fetal breathing movements were not inhibited by maternal smoking. Cardiovascular responses of fetuses of smoking mothers were significantly less during labor than reponses of fetuses of nonsmoking controls. The baboon can be studied under relatively stable chronic conditions, and measurements of fetal heart rate, breathing movements, and carotid blood flow can be obtained under controlled conditions. Changes in breathing movements that occur under various conditions mimic those found in humans. Sensitivity of atrial rate to acetylcholine decreases as fetal development progresses, and adrenergic innervation of fetal right atria is essentially the same over gestational periods studied. Villous capillary basement membrane thickness in smokers averaged 142 percent of controls and trophoblastic basement membrane was 165 percent of controls. Fetal weight was significantly reduced in rats in the experimental group. The greatest effects were seen in the lung and liver; both showed a significant decrease in total weight, DNA, RNA, and protein.

Future Plans:
The causes of reduced fetal weight and differential fetal growth will be investigated.

Project Dates:
August 1979–July 1985.

Financial Support:
NICHD (HD 13063).

1229. COLUMBIA UNIVERSITY, 630 West 168th Street, New York, New York 10032.

Project Title:
Smoking and Pregnancy and Subsequent Child Development (British Children).

Principal Investigator:
Rush, D.

Objective:
To determine the effect of maternal smoking on subsequent child development.

Methods or Approach:
All singletons born during 1 week in Great Britain (10,327) were followed up at age 5, controlling for parental social, economic, and educational status; maternal developmental history; psychosomatic symptoms and attitudes toward childrearing; and child's exposure to preschool education. Developmental outcomes included Copy Designs Test, English Picture Vocabulary Test, Human Figure Drawing Test, height, head circumference, antisocial behavior, enuresis/encopresis, activity level, and neurotic symptoms.

Results to Date:
Smoking during pregnancy was associated with depressed somatic growth (height, -.66 cm, $p < 0.001$), enuresis/encopresis, and antisocial behavior ($p < 0.01$). Differences in mental ability were small and overactivity remained barely significant. Entire effect on head circumference and 49 percent of effect on height were accounted for by reduced birth weight associated with maternal smoking.

Financial Support:
NICHD (5R01HD13347-04).

1230. COLUMBIA UNIVERSITY, 701 West 168th Street, New York, New York 10032.

Project Title:
Development of Monoclonal Antibodies to Carcinogen Adducts.

Principal Investigator:
Santella, R.

Objective:
To develop monoclonal antibodies that react specifically with protein modified by a diol epoxide derivative of benzo(*a*)pyrene (BPDE I); utilize the antibodies in a highly sensitive enzyme-linked immunoassay (ELISA) to quantitate levels of BaP in human hemoglobin.

Methods or Approach:
Mice will be immunized with BPDE I-modified hemocyanin; spleen cells will be fused with myeloma cells to produce hybrids secreting specific antibody. An ELISA will be developed using monoclonal antibodies to quantitate levels of BaP on protein. Hemoglobin isolated from human red blood cells will be assayed for adducts.

Results to Date:
Several clones that produce antibody specific for BPDE I-modified protein have been isolated.

Project Dates:
July 1984–June 1987.

Financial Support:
CTR.

1231. COLUMBIA UNIVERSITY, COLLEGE OF PHYSICIANS AND SURGEONS, 622 West 168th Street, New York, New York 10032.

Project Title:
Fetal Activity and Response to Hypoxia During Development.

Principal Investigators:
James, L.S.; Stark, R.I.; Daniel, S.S., et al.

Objective:
To determine effect of maternal smoking on fetal oxygenation, activity, and behavior; define neuroendocrine effects of cigarette smoke and its components on the fetus.

Methods or Approach:
Studies are conducted in chronically instrumented fetal sheep and baboons. Sheep are studied to define effects of cigarette smoke components on fetal concentrations of β-endorphin and vasopressin in plasma and cerebrospinal fluid. Baboons are examined for effects of cigarette smoke (mothers are conditioned to smoke) on fetal activities (blood pressure, heart rate, breathing movements, EEG) and biochemical indices of oxygenation.

Results to Date:
Study models have been established. Alterations in fetal behavior are apparent with nicotine infusion to the mother. Morphologic changes in placenta of chronically smoking baboon mothers have been noted.

Project Dates:
August 1985–July 1990.

Financial Support:
NICHD (P50).

1232. COLUMBIA UNIVERSITY, SCHOOL OF PUBLIC HEALTH, 630 West 168th Street, New York, New York 10032. UNIVERSITY OF CHICAGO, National Opinion Research Center, 6030 S. Ellis Avenue, Chicago, Illinois 60637.

Project Title:
Family Processes in Adolescent Drug Use, Wave 3.

Principal Investigator:
Kandel, D.
Objective:
To investigate the relative importance of parents and peers on drug use (including smoking); identify the nature of families in which drug use develops and is promoted.
Methods or Approach:
In the third wave of a longitudinal study of a sample of youth in New York State that was started in 1971, questions were asked on social networks that support drug use, with the focus on the families, friends, and spouses of respondents. Self-administered questionnaires were left with spouses or partners. Telephone interviews were conducted with a subsample of 1,222 of the original respondents who also participated in the previous wave in 1980.
Results to Date:
Response rate for the 1984 wave was 93 percent.
Financial Support:
NIDA.

1233. CORNELL UNIVERSITY MEDICAL COLLEGE, 411 East 69th Street, New York, New York 10021.

Project Title:
Factors Inhibiting Drug Use: Teacher and Peer Effects.

Principal Investigator:
Botvin, G.J.
Objective:
To (1) gain a better understanding of factors inhibiting or preventing onset and early stages of tobacco, alcohol, and marijuana use; (2) test efficacy of a comprehensive psychosocial substance abuse prevention strategy when implemented by regular classroom teachers or peer leaders; and (3) test relative effectiveness of "booster" sessions.
Methods or Approach:
Ten schools (n=1,200) were randomly assigned to either (1) teacher administered intervention; (2) peer administered intervention; (3) teacher administered intervention plus booster sessions; (4) peer administered intervention plus booster sessions; or (5) pretest–multiple posttest control. All groups were pretested, followed by intervention (20 sessions) for the four experimental groups. There will be six posttests for all groups; at end of intervention and at 6, 12, 18, 24, and 36 months.
Results to Date:
First year results indicate that the prevention program had a significant impact on cigarette smoking ($p<0.03$), excessive alcohol use ($p<0.006$), and marijuana use ($p<0.006$) when implemented by peer leaders. The most dramatic impact was on marijuana use; for students in the peer-led condition, total marijuana use was reduced by 71 percent and regular (weekly or daily) use by 83 percent. Effectiveness was also evident with respect to several cognitive, attitudinal, and personality variables. Students in the peer-led condition had significantly higher posttest scores on the three knowledge measures ($p<0.0001$) and had significantly higher antismoking ($p<0.01$), antidrinking ($p<0.0001$), and antimarijuana ($p<0.0001$) posttest attitude scores than controls. Treatment effects were also evident with respect to susceptibility to influence regarding smoking ($p<0.001$). In addition, students in the peer-led condition rated themselves as being significantly less likely to be influenced by peers to smoke cigarettes than students in the control condition or in the teacher-led condition. Results support the effectiveness of a broad-spectrum substance abuse prevention strategy that focuses primarily on teaching students generic life skills and skills related more directly to resisting social pressures to smoke, drink excessively, or use marijuana.
Project Dates:
December 1980–1985.
Financial Support:
NIDA (DA 02835).
Reference:
Botvin, G.J.; Renick, N.L.; Filazzola, A.D., et al. "A Cognitive-Behavioral Approach to Substance Abuse Prevention." *Addictive Behaviors* 9:137-147, 1984.

1234. CORNELL UNIVERSITY MEDICAL COLLEGE, 411 East 69th Street, New York, New York 10021.

Project Title:
Cancer Risk Reduction Through Smoking Prevention.

Principal Investigator:
Botvin, G.J.
Objective:
To (1) test the efficacy of a multicomponent psychosocial school-based smoking prevention strategy; (2) determine relative effectiveness of the smoking prevention curriculum with/without additional intervention activities targeted at the larger school environment; (3) test effectivesness of this strategy with urban students from minority and lower socioeconomic status families and with suburban middle-class populations; (4) determine extent to which preventive gains produced in the first year can be sustained over the course of junior high school; (5) determine any sex differences in relative effectiveness of prevention strategy; and (6) determine extent to which reductions in new cigarette smoking are related to changes in specific cognitive, attitudinal, and personality variables.
Methods or Approach:
Seventh graders (n=6,000) in the 22 urban and suburban schools participating (greater New York City area) were randomly assigned to (1) smoking prevention curriculum alone; (2) smoking prevention curriculum plus school-wide support activities designed to reinforce and help maximize program effectiveness; or (3) control group. All groups were pretested; 20 sessions followed for intervention groups. Posttest will occur every year for 3 years.
Results to Date:
Results are being analyzed.
Project Dates:
August 1983–1986.
Financial Support:
NCI (CA 33[illegible]17).

1235. CORNELL UNIVERSITY MEDICAL COLLEGE, 411 East 69th Street, New York, New York 10021.

Project Title:
Longitudinal Evaluation of Life Skills Training.

Principal Investigator:
Botvin, G.J.
Objective:
To (1) provide a rigorous evaluation of the long-term effective-

ness of a psychosocial smoking prevention strategy called Life Skills Training; (2) assess effectiveness of the smoking prevention curriculum with either live teacher training and ongoing support by research staff or with video-taped teacher training and minimal support by research staff; (3) measure impact of school climate on program effectiveness; (4) examine relative effectiveness of the curriculum on high-risk students; and (5) examine cost effectiveness of the program.

Methods or Approach:
Schools (n = 45) from three regions of New York State will be randomly assigned to (1) intensive involvement (live teacher training and staff support); (2) minimal involvement (videotaped teacher training and minimal staff support); or (3) control. A modified multiple time series design will be utilized. Measurements will be taken pre- and postintervention. Follow-up will include questionnaires and collection of carbon monoxide samples.

Results to Date:
Project is in a preliminary phase.

Project Dates:
December 1984–1989.

Financial Support:
NHLBI (HD 33865).

1236. CUSTOM SUPPLEMENTS, INC., 201 East 66th Street, Suite 17M, New York, New York 10021.

Project Title:
A Nutritional Approach to Continued Cigarette Smoking.

Principal Investigator:
Goldman, B.

Objective:
To create a book for mass distribution that will describe to cigarette smokers what they can do to enhance their immune system to better deal with the latent hazards of cigarette smoking.

Methods or Approach:
A worldwide literature search of magazine, journal, and newspaper articles has been conducted and computer probes for published information have been made.

Results to Date:
Cadmium levels are high in smokers, affecting bodily adsorption and utilization of zinc, which may be the most important trace mineral in the body. Smokers, if they cannot quit, are encouraged to learn more about the nutritional problems related to smoking and to adjust their diet to compensate for nutritional deficiencies.

Future Plans:
Attempts will continue to have the book published.

Project Dates:
1976–1986.

1237. FRANKLIN DELANO ROOSEVELT VETERANS ADMINISTRATION HOSPITAL, Montrose, New York 10548.

Project Title:
Quit by Mail: An Outreach Smoking Cessation Program.

Principal Investigator:
Schneider, S.J.

Objective:
To develop and evaluate a stop smoking program that employed computerized direct mail to recruit smokers and distribute personalized behavioral smoking cessation treatment materials.

Methods or Approach:
Treatment occurs through interactions by mail between smokers and the computer, which proceed anonymously and conveniently. Treatment was intended to bring about complete abstinence within 4 weeks, using mailed interactions tailored specifically to the smoking characteristics and progress of each participant. A total of 1,044 daily smokers were asked to attend face-to-face smoking cessation treatment, and those who wished to do so were offered such sessions. Those who did not wish to do so were randomly assigned to three other groups: (1) interactive computerized direct mail treatment; (2) handbook that provided smoking cessation instructions in noninteractive, nonpersonalized format; and (3) several stop smoking pamphlets but no behavioral treatment.

Results to Date:
Only 11.2 percent wished to participate in face-to-face treatment; however, 21.2 percent of those assigned to the computerized mail group participated in treatment when it was offered. Abstinence rates for subjects in the computerized program and those in the face-to-face groups were similar. Subjects in the face-to-face group tended to quit earlier in treatment than those in the computerized mail group. Reduction in consumption occurred more often in face-to-face and computerized mail groups. Women were more likely than men to participate in either group when it was offered.

Project Dates:
January 1980–completed.

Financial Support:
VA.

1238. HEALTH RESEARCH INC., 666 Elm Street, Buffalo, New York 14263.

Project Title:
Effects of Nicotine on the Carcinogenic Activity of Smoke Condensate From Experimental Cigarettes.

Principal Investigators:
Tso, T.C.; Fox, H.

Objective:
To determine whether nicotine is a cocarcinogen in tobacco smoke.

Methods or Approach:
Using both bright and burley tobacco types with low nicotine content (0.2-0.4 percent), different levels of pure nicotine will be added to establish three different levels of nicotine. Experimental materials will be reconstituted into sheets, and experimental cigarettes will be made for short-term bioassay using the sebaceous gland suppression method. Long-term mouse skin painting will be conducted to test carcinogenic activity.

Results to Date:
Condensates from bright tobacco cigarettes exhibited twice as much carcinogenic activity as did condensates of burley cigarettes. The activity of the burley condensates depended on the nicotine content of the cigarette, whereas the activity of the bright condensates did not. The smoke condensates from the six cigarette types fell into two clearly distinguishable series. Flue-cured tobacco delivered 22 to 26 mg of smoke condensate/cigarette, whereas the cigarettes of burley tobacco delivered from 9 to 10 mg of condensate. The nicotine concentration of low-nicotine burley condensate was about three times that of the low-nicotine flue-cured condensate, but both were relatively low. Benzopyrene levels were not greatly different among the samples of the same tobacco type, but were about 50 percent higher in burley condensates than in flue-cured condensates. There appeared to be a nicotine-dependent

increase in sebaceous gland suppression in burley, but not in flue-cured condensates. In all cases, more tumors were produced by the higher dose; differences were statistically significant in half of the comparisons.

Project Dates:
March 1979–November 1983.

Financial Support:
USDA (1090-20881-001C).

Reference:
Bock, F.C.; Tso, T.C.; Fox, H. "The Effect of Nicotine Level in Tobacco on the Carcinogenic Activity of Cigarette Smoke Condensate." In: Proceedings of the International Union Against Cancer, Seattle, Washington, 1982.

1239. LENOX HILL HOSPITAL, 100 East 77th Street, New York, New York 10021.

Project Title:
Effect of Nicotine Administration on Colitis.

Principal Investigator:
Korelitz, B.I.

Objective:
To determine the effect of administering nicotine in the form of chewing gum to colitis patients.

Methods or Approach:
Patients will be grouped as (1) ex-smokers or (2) nonsmokers and given either nicotine or placebo gum for 1 month. Treatments will then be crossed. Daily dose will be increased and decreased gradually. Patients will be informed of potential value and potential risk of the study and signed permission will be obtained. Criteria for diagnosis of ulcerative colitis will be documented, and followup sigmoidoscopies after initiating nicotine or placebo gum treatment will be performed at 2 weeks and 1 month. Patients will keep stool charts during both arms of the study and patients will be dropped if the disease worsens to a degree that new medication has to be introduced, if the patient wishes to withdraw, or if compliance is inadequate.

Results to Date:
Project is in a preliminary phase.

Project Dates:
November 1984–October 1985.

Financial Support:
CTR.

1240. MEDICAL FOUNDATION OF BUFFALO, INC., 73 High Street, Buffalo, New York 14203.

Project Title:
Aromatase Inhibitors in Cigarette Smoke and Tobacco.

Principal Investigator:
Osawa, Y.

Objective:
To (1) isolate active ingredients in cigarette smoke and tobacco extracts that suppress estrogen production by human placental aromatase in in vitro assays; (2) define modes of aromatase inhibition or inactivation; (3) determine molecular structures of ingredients; (4) evaluate in vivo suppressive effects on breast carcinomas and estrogen production in experimental animals; and (5) assess potential for use for steroid enzymology, endocrinology, and medicinal application.

Methods or Approach:
To isolate aromatase inhibitors, solvent extraction and partition are used to separate ingredients into neutral, acid, phenolic, basic, and aqueous polar fractions. Fractions containing active components are further purified by various combinations of chromatography, distillation, and recrystallization. To determine structure and kinetic nature of the inhibitors, purified active components will be subjected to physicochemical analyses. Kinetic analysis of aromatase inhibition will be conducted by use of a selective (^{3}H)water method to determine whether it is competitive, irreversible, or based on an enzymatic mechanism. For in vivo assessment, purified active ingredient will be given to a group of rats with breast carcinomas (BUF/N rats induced with NMU) and suppression of tumor growth and ovarian function will be evaluated and compared with castrated, vehicle-only controls and synthetic aromatase inhibition groups.

Results to Date:
Cigarette smoke and alcohol extract of tobacco leaves were found to have a dose-response inhibitory effect on aromatase activity. A 0.07 cigarette equivalent of methylene chloride extract of cigarette smoke and a 0.025 cigarette equivalent of 70 percent ethanol extract of tobacco leaves showed 50 percent inhibition of human placental aromatase (85 to 98 pmol estrogen/min activity/assay). The inhibitory activity in cigarette smoke was concentrated into the basic fraction and inhibitors from tobacco leaves were separated into acid and basic fractions. Nicotine and cotinine were ruled out as major inhibitors by chromatographic behavior and weak specific inhibition activity. Kinetic analysis of active fractions indicated that basic inhibitors act competitively against androstenedione aromatization, but acidic inhibitors in tobacco leaves inactivate aromatase irreversibly.

Future Plans:
Plans include (1) isolation and structure determination of major inhibitory components in tobacco leaves and cigarette smoke; (2) studies on the mechanism of aromatase inhibition by tobacco components; and (3) evaluation of in vivo effects of aromatase inhibitors in cigarette smoke and tobacco in small animal models.

Project Dates:
January 1984–December 1986.

Financial Support:
CTR.

1241. MEMORIAL HOSPITAL FOR CANCER AND ALLIED DISEASES, 1275 York Avenue, New York, New York 10021.

Project Title:
Screening for Early Lung Cancer by Chest X-Rays and Sputum Cytology.

Principal Investigator:
Melamed, M.R.

Objective:
To determine whether screening by annual PA and lateral chest x rays and sputum cytology every 4 months will lead to early detection and treatment of lung cancer in a high-risk population (men over 45 years old who smoke cigarettes), and result in a lowered death rate for that disease.

Methods or Approach:
Volunteers, 10,040 men over 45 years old who smoke cigarettes, were recruited into this study. They were examined annually by full-size PA and lateral chest x rays taken on a 140 KV machine. About half the men, randomly selected, also had sputum cytology examinations every 4 months. Every effort was made to investigate suspicious radiologic or cytologic findings, and to treat any detected lung cancers as promptly as possible. The entire population was carefully monitored to determine whether this program had a favorable effect on the mortality rate from lung cancer.

Results to Date:
At this time there have been a total of 288 lung cancers identified; 117 (about 41 percent) were found "early," (in A.J.C. Stage I). The overall 5-year survival for early-stage lung cancer is 70 percent. The Stage II and III lung cancer cases have a survival of about 5 percent at 5 years. Approximately 18 percent of the newly developing carcinomas in this population were oat cell carcinoma, and 88% (38/43) were advanced at the time of diagnosis. These results suggest that oat cell carcinoma cannot be detected early by present techniques but that with a carefully conducted program of chest x rays and sputum cytology, it is possible to identify from 40 to 60 percent of non-oat cell lung cancers at an early and potentially curable stage.

Future Plans:
The screening phase of this program was completed in October 1982; the followup phase will conclude in December 1984.

Project Dates:
September 1973–December 1984.

Financial Support:
NCI (NO 1 CB45007).

Reference:
Melamed, M.R.; Flehinger, B.J.; Zaman, M.B., et al. "Screening for Early Lung Cancer. Results of the Memorial Sloan-Kettering Study in New York." *Chest* 86(1):44-53, July 1984.

1242. METROPOLITAN LIFE INSURANCE CO., 330 Park Avenue South, New York, New York 10010.

Project Title:
Industrywide Network for Social, Urban, and Rural Efforts Project on Lifecycle Preventive Health Services.

Principal Investigators:
Logston, D.N.; Rosen, M.A.; Lazaro, C., et al.

Objective:
To (1) measure long-term improvements in behavioral risk factors and selected health outcomes among study patients (i.e., smoking cessation); (2) further develop the physician education module for health promotion and disease prevention in primary medical care; (3) increase operational effectiveness of the Lifecycle model among study physicians; (4) implement efficient followup system for maintenance of behavioral risk factor reduction among study patients; (5) determine costs and utilization patterns for preventive services on a longitudinal basis and in different health care settings; and (6) define the potential effects on health insurance and cost containment.

Methods or Approach:
A quasi-experimental design was utilized in three study sites where the Lifecycle model has been implemented, and matched with similar control group practice sites. The design included 750 well patients stratified across 10 age groups and 18 primary care physicians at each of the group practice sites, for a total sample size of 4,300 study patients. Pre- and postintervention surveys of primary care physicians and patients were conducted at baseline and at 12 months. Intervention consists of educating study physicians to use the Lifecycle model with patients. Age-specific guidelines were formulated into study protocols, and patient encounter forms were developed to remind physicians of the protocols and to collect medical data. A "prevention prescription," completed by the physician (including recommendations for risk factor reduction), was given to the patient at the time of the visit. Patient guides, with information on the purpose of the preventive visit, self-administered risk assessments, and followup instructions were provided for patients at each study site, in addition to an array of recommended health education pamphlets on changing health-related behavior. INSURE assumed financial responsibility for the preventive visits by patients as part of the Lifecycle model.

Results to Date:
Findings, based on pre- and postintervention surveys, indicate that physicians made effective use of the Lifecycle model following special continuing medical education training and development of a payment mechanism for preventive services that included patient education on risk factor reduction. Adult patients at risk changed health-related behavior in excess of changes among reference-site patients in regard to smoking cessation, beginning regular exercise, always using seat belts, regular breast self-examination, weight loss, and decreased alcohol intake. Changes in health-related behavior by children and adolescents at study sites also exceeded changes among reference-site patients. The average cost in charges for the Lifecycle preventive services, including patient education, appears manageable. Results suggest that preventive services in primary medical case are feasible, patients will improve health-related behavior, and costs are controllable.

Future Plans:
The Lifecycle model will be evaluated in health maintenance organizations and other prepaid medical practices. The insurability and long-range effects of health promotion and disease prevention on cost containment will be investigated.

Project Dates:
1980–1987.

Financial Support:
Robert Wood Johnson Foundation.

1243. METROPOLITAN LIFE INSURANCE COMPANY, One Madison Avenue, New York, New York 10010.

Project Title:
Preventive Medicine in the Corporate Setting.

Principal Investigators:
Arnold, C.B.; Cunningham, L.; Mushinski, M.

Objective:
To identify the proportion and distribution of diagnosis-related groups (DRGs) that are related to tobacco use and other preventable risk factors among a large insured population across the United States; develop a health behavior inventory and a health prospects appraisal form for use in corporate settings to encourage the concept of employee wellness.

Methods or Approach:
Hospital claims data will be analyzed by DRG, state, and region and divided into categories according to the estimated contribution made by tobacco, alcohol, nutrition, exercise, and stress to prevalence of disease groups. A health behavior inventory will document the degree to which various risk factors exist in corporate settings and provide baseline data to measure effectiveness of specially developed intervention techniques. A model will be developed toward the ultimate goal of decreasing corporate medical care costs and more effective utilization of medical resources.

Results to Date:
Study design, weighting procedures, and health inventory are currently being pretested; data analysis will begin in mid-1985.

Project Dates:
February 1985–continuing.

Financial Support:
Metropolitan Life Insurance Company.

1244. MOUNT SINAI MEDICAL CENTER, ENVIRONMENTAL SCIENCES LABORATORY, 10 East 102 Street, New York, New York 10029.

Project Title:
Lead Cadmium and Arsenic Absorption in Copper Smelter Workers.

Principal Investigator:
Lilis, R.

Objective:
To assess exposure and absorption of lead, cadmium, and arsenic (contaminants of copper ore) in copper smelter workers; determine health effects related to metal body burden.

Methods or Approach:
A cross-sectional medical examination of a copper smelter workforce included determination of blood lead (Pb-B), zinc protoporphyrin (ZPP), blood cadmium (Cd-B), urinary cadmium (Cd-U), and urinary arsenic (As-U), since it was known that such metal impurities were present in copper concentrate. A total of 680 active employees and 96 retirees and ex-employees were examined. Another 144 men, never employed in the smelter but had worked in copper mines (and sometimes gold mines), were also examined.

Results to Date:
Mean Pb-B, ZPP, Cd-B, and As-U were significantly higher in active copper smelter employees than in retirees or miners, indicating exposure and absorption in the smelter. Significant correlations between Pb-B and Cd-B and between Cd-U and As-U were present, confirming the common source of absorption. Although there was evidence for increased lead absorption, this was very moderate, with practically no Pb-B levels in excess of 60 μg/dL. Smoking is known to be an important factor in cadmium absorption and body burden; Cd-B was found to be significantly higher in smokers in all subgroups, and was shown to have a much larger effect on Cd-U and Cd-B levels than in other studies addressing this problem. The highest levels of Cd-U were found in retirees, specifically retirees who smoked. The significantly higher Cd-B levels in smokers were definitely not related to age, indicating the independent contribution of exposure to cadmium. Cd-U did not exceed 10μg/g creatinine, the generally accepted critical level for the kidney, but was higher than 2 μg/g creatinine, a level very rarely exceeded in the general population.

Financial Support:
NIEHS (ES 00928).

References:
(1) Lilis, R.; Valciukas, J.A.; Weber, J.-P., et al. "Distribution of Blood Lead, Blood Cadmium, Urinary Cadmium, and Urinary Arsenic Levels in Employees of a Copper Smelter." *Environmental Research* 33:76-95, 1984. (2) Lilis, R.; Valciukas, J.A.; Weber, J.-P., et al. "Epidemiologic Study of Renal Function in Copper Smelter Workers." *Environmental Health Perspectives* 54:181-192, 1984.

1245. MOUNT SINAI SCHOOL OF MEDICINE, 5th Avenue and 100th Street, New York, New York 10029.

Project Title:
Role of the Father in His Son's Drug Use.

Principal Investigators:
Brook, D.W.; Brook, J.S.

Objective:
To study the father's role in his adolescent son's use of tobacco and marijuana.

Methods or Approach:
The sample consists of 250 male adolescents and their fathers. Self-administered questionnaires were given in the fall of 1979 and spring of 1980. The study has two foci: (1) a specification of paternal factors (e.g., paternal personality/attitudinal attributes, paternal child-rearing practices, and the extent to which the father serves as a role model for his son) which may influence his son's drug behavior; and (2) an interrelationship approach which requires examination of the paternal dimensions alone and in interaction with the adolescent's own personality and the family system. The paternal factors alone and in interaction will be examined in relation to the son's choice of drugs and mild vs. heavy use of tobacco and marijuana.

Results to Date:
Results have been published.

Project Dates:
June 1979–December 1981.

Financial Support:
NIDA (5RO1 DAO2390-03).

References:
(1) Brook, J.S.; Whiteman, M.; Gordon, A.S. "Role of the Father in His Son's Marijuana Use." *Journal of Genetic Psychology* 138:81-86, 1981. (2) Brook, J.S.; Whiteman, M.; Gordon, A.S. "Maternal and Personality Determinants of Adolescent Smoking Behavior." *Journal of Genetic Psychology* 139:185-193, 1981. (3) Brook, J.S.; Whiteman, M.; Brook, D., et al. "Paternal Determinants of Male Adolescent Marijuana Use." *Developmental Psychology* 17(6):841-847, 1981. (4) Brook, J.S.; Whiteman, M.; Gordon, A.S., et al. "Fathers and Sons: Their Relationship and Personality Characteristics Associated With the Son's Smoking Behavior." *Journal of Genetic Psychology* 142:271-281, 1983. (5) Brook, J.S.; Whiteman, M.; Gordon, A.S. "Stages of Drug Use in Adolescence: Personality, Peer, and Family Correlates." *Developmental Psychology* 19:269-277, 1983. (6) Brook, J.S.; Brook, D.; Whiteman, M., et al. "Depressive Mood in Male College Students: Father-Son Interactional Patterns." *Archives of General Psychiatry* 40:665-669, 1983. (7) Brook, J.S.; Whiteman, M.; Gordon, A.S., et al. "Paternal Correlates of Adolescent Marijuana Use in the Context of the Mother-Son and Parental Dyads." *Genetic Psychology Monographs* 108:197-213, 1983. (8) Brook, J.S.; Whiteman, M.; Gordon, A.S., et al. "Identification with Paternal Attributes and Its Relationship to the Son's Personality and Drug Use." *Developmental Psychology* 20:1111-1119, 1984.

1246. MOUNT SINAI SCHOOL OF MEDICINE, One Gustave L. Levy Place, Annenberg 22-74, New York, New York 10029.

Project Title:
Role of Father/Mother/Sibling in Adolescent Drug Use.

Principal Investigators:
Brook, J.S.; Brook, D.W.

Objective:
To (1) prepare a monograph on the etiology of adolescent marijuana use based on findings from three data sets (two on father/child and one on mother/child); (2) study the role of the sibling in adolescent drug use, specifically the relationship between brothers; and (3) utilize data from an earlier father/son study to compare father's and older brother's role in an adolescent's development and drug use.

Methods or Approach:
Research is continuing on the role of parents, personality, and peers in adolescent use of tobacco, alcohol, marijuana, amphetamines and barbiturates (prescribed and nonprescribed), and illicit drugs other than marijuana. Cross analyses of three data

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sets will permit indepth analyses of the interrelations of parent, adolescent, marital harmony, and peer domains, and interactions of specific variables from these domains to see how various factors affect adolescent marijuana use. For the sibling study, questionnaires (given to 300 male college students and their older brothers) will include a number of scales with adequate psychometric properties designed to tap crucial personality, peer, parental, and sibling variables. A detailed series of questions on licit and illicit drug use will also be included. Hierarchical multiple regression will be the primary analytical technique employed.
Results to Date:
Project is in a preliminary phase.
Project Dates:
July 1984–June 1989.
Financial Support:
NIDA (DA-02390-08).

1247. MOUNT SINAI SCHOOL OF MEDICINE, Department of Pathology, One Gustave L. Levy Place, New York, New York 10029.

Project Title:
Lung Proteases and Antiproteases in Coal Dust Exposure.

Principal Investigators:
Ip, M.P.C.; Kleinerman, J.
Objective:
To test the hypothesis that elastases secreted by alveolar macrophages (AMs) and PMNs following in vivo exposure of small laboratory animals to coal dust will create focal or diffuse emphysema, or fibrosis associated with coal workers pneumoconiosis (CWP).
Methods or Approach:
Effect of nitrogen dioxide, an important component of cigarette smoke, will also be studied in conjunction with coal dust exposure to evaluate the effect of combined injury on protease and antiprotease balance and on potential to produce lesions of simple CWP, including focal emphysema. Lung pathology and histology studies by light and electron microscopy will be used to determine whether pathological lesions characteristic of CWP and focal emphysema develop following multiple instillation of coal dust at time periods of 3 days and 90 days after the last exposure. Type and amount of reactive oxygen metabolites generated will be measured both in vivo and in vitro to determine if these products can inactivate alveolar antiproteases. Studies are performed in hamsters given single or multiple intratracheal instillations of respirable coal dust particles. Importance of contributory elements that govern pathogenesis of focal emphysema seen in simple CWP are determined biochemically or histologically on either lung tissues or lung lavage fluid collected on sacrifice. Parameters include biochemical analysis of lung elastase, antiproteases, lung morphology, and lung histology. Activities of reactive oxygen metabolites generated from AMs or PMNs are also studied. Results are compared with those from control animals to determine whether the factors are important in pathogenesis of simple CWP.
Results to Date:
Single or multiple instillation of coal dust particles induces rapid infiltration of AMs and PMNs into alveoli. Total lung elastolytic burden is increased. Single exposure to increasing amount of coal dust particles (up to 4 mg) does not induce increase in alveolar antiprotease levels. Functional activities of alveolar antiproteases remain unaltered. Multiple instillation of a total of 40 to 62 mg coal (5 instillations in 4 to 5 weeks) induces a greater increase in PMN while the total number of AMs also increases, indicating that cellular response of the lung to multiple instillation may be different from that induced by a single injection. Intratracheal introduction of coal is accompanied by a marked increase in alveolar antiproteases concentrations, implying that protease and antiprotease alteration may play a role in development of coal-induced lung lesions.
Project Dates:
May 1984–April 1986.
Financial Support:
NIOSH (0H01715-02).

1248. MOUNT SINAI SCHOOL OF MEDICINE, One Gustave L. Levy Place, Annenberg 22-74, New York, New York 10029.

Project Title:
Childhood Etiologic Determinants of Adolescent Drug Use.

Principal Investigators:
Brook, J.S.; Cohen, P.
Objective:
To explore how sets of early childhood and early and later adolescent attributes interrelate in their impact on involvement (or noninvolvement) in stage of drug use over time; examine changes in personality and behavior and in family and peer relationships as a consequence of marijuana use.
Methods or Approach:
Mothers in the sample were interviewed when the children were 3 to 10 years of age; both mothers and children were interviewed again when the children were 11 to 18 years of age. The cohort will be interviewed again (separate interviews in the home) when children are 13 to 20 years of age. Scales with adequate psychometric properties measuring independent variables will be developed from interview schedules. The primary analytic technique will be hierarchical multiple regression or causal analysis. Drug use groups will be established based on stages of drug use. A stage frequency variable will be created, based not only on stage of use, but also on frequency of use at each stage. There may be significant differences between two individuals at the same stage of drug use if one is merely experimenting with a drug while the other is already a heavy user of marijuana. A stage approach allows (1) treatment of all drugs in one conceptual framework and (2) isolation of factors that are associated with being at risk for each of the stages and those that are associated with movement in stage of use over time.
Results to Date:
Three distinct developmental stages in involvement in drug use have been identified: (1) legal drugs (cigarettes or hard liquor); (2) marijuana; and (3) illicit drugs other than marijuana.
Future Plans:
A home observation study is planned of cohort offspring (at least 12 months old), including motor, mental, and behavioral development and relationships with their young parents.
Project Dates:
September 1982–November 1987.
Financial Support:
NIDA (DA 03188-03).
Reference:
Brook, J.S.; Whiteman, M.; Gordon, A.S., et al. "Dynamics of Childhood and Adolescent Personality Traits and Adolescent Drug Use." Paper presented at the Annual Meeting of the American Academy of Child Psychiatry, October 1984.

1249. NASSAU HOSPITAL, Pulmonary and Critical Care Section, 259 First Street, Mineola, New York 11501.

Project Title:
The Role of Bacterial Adherence in Colonization of the Airways of Patients With Chronic Lung Disease.

Principal Investigators:
Niederman, M.S.; Grant, M.M.; Shoch, P., et al.
Objective:
To examine the pathogenetic role of bacterial adherence in gram-negative bacillary colonization of the lower respiratory tract of smokers and nonsmokers with chronic lung disease.
Methods or Approach:
Patients with a variety of chronic lung diseases including chronic bronchitis, emphysema with respiratory failure, and neuromuscular respiratory failure will be studied. Tracheal cells will be collected bronchoscopically and bacterial adherence measured using *Pseudomonas aeruginosa* in a radiometric assay. Patient nutritional status will be evaluated and colonization patterns of patients will be related to adherence data. Microenvironmental influences in the airway will be studied by relating airway pH, immunoglobulin, and protease levels of adherence and colonization data.
Results to Date:
Human tracheal cells can bind gram-negative bacilli, but normal smokers and nonsmokers have similar degrees of adherence to lower airway cells. However, patients with chronic lung disease, especially those with *Pseudomonas* species colonization, have higher tracheal cell adherence than subjects without disease. Microenvironmental factors that affect adherence and may be amenable to modification include host nutritional status (decline leads to increased adherence), airway pH and elastase activity (increase leads to enhanced adherence), and airway immunoglobulin A (decline leads to increased adherence).
Future Plans:
Patients with other lung diseases will be examined to see whether secretions from smokers have a specific effect on adherent properties of cells collected from nonsmokers.
Project Dates:
January 1985–continuing.
Financial Support:
Nassau Hospital.

1250. NATHAN S. KLINE INSTITUTE, CENTER FOR NEUROCHEMISTRY, Ward's Island, New York, New York 10035.

Project Title:
Comparison of (^{3}H)Nicotine and (^{3}H)Acetylcholine Binding in Several Strains of Mice.

Principal Investigators:
Sershen, H.; Reith, M.E.A.; Lajtha, A.
Objective:
To measure regional binding of (^{3}H)nicotine and (^{3}H)acetylcholine (a ligand with an expected cholinergic profile) in C57/BL and DBA mice; examine inhibition of (^{3}H)nicotine binding by nicotine and acetylcholine.
Methods or Approach:
Adult male C57/BL and DBA mice were decapitated, and brain regions were rapidly removed and homogenized in 5 mL of 50 mmol Tris buffer containing 1.5 μM atropine sulfate (to block muscarinic sites) when binding of (^{3}H)acetylcholine was measured. Tissue was washed and homogenized in fresh buffer, and the final pellet was suspended in buffer at a concentration of about 1 mg protein/0.5 mL. For the acetylcholine binding assay, buffer contained 100 μM eserine to prevent hydrolysis of acetylcholine. Samples of membrane homogenate were incubated at 0° C for 15 minutes with 15 nmol (±)-(^{3}H)nicotine with or without 4 mmol nicotine for defining nonspecific binding, or with 19 nmol (^{3}H)acetylcholine with or without 100 μmol carbachol for nonspecific binding.
Results to Date:
The relative amount of nicotine binding and acetylcholine binding in various brain regions was determined. Although midbrain showed the highest and cerebellum the lowest binding for both (^{3}H)nicotine and (^{3}H)acetylcholine, the ratio of nicotine to acetylcholine binding showed a threefold regional variation. Acetylcholine inhibition of (^{3}H)nicotine binding indicated that a portion of nicotine binding was not inhibited by acetylcholine. Results indicate that there are important differences between binding of (±)-(^{3}H)nicotine and of (^{3}H)acetylcholine.
Future Plans:
Results indicate that a portion of (^{3})nicotine binding occurs at sites distinct from those for acetylcholine. Further pharmacological characterization of these sites is needed to assess whether they play a functional role in some of the actions of nicotine.
Project Dates:
January 1983–December 1984.
Financial Support:
CTR.

1251. NATHAN S. KLINE INSTITUTE, CENTER FOR NEUROCHEMISTRY, Ward's Island, New York, New York 10035.

Project Title:
Development of an Animal Model of Parkinson's Disease.

Principal Investigators:
Sershen, H.; Reith, M.E.A.; Lajtha, A.
Objective:
To test the possible ameliorating effects of nicotine and/or cigarette smoke components on observed biochemical alterations of dopaminergic and related pathways by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in mice.
Methods or Approach:
MPTP has been shown to give rise to severe Parkinsonism in humans and like symptoms in monkeys, as a result of nerve cell degeneration in the substantia nigra. Epidemiological studies suggest that cigarette smoking may have a beneficial effect on progress of Parkinson's disease, but pharmacological reasons for this effect are as yet unknown. To test for possible ameliorating effects of nicotine and/or cigarette smoke components, BALB/cBy mice were injected with MPTP (8 mg/kg, retro-orbital or via tail vein). Dopaminergic function was assayed by measuring labeled dopamine uptake into isolated striatal synaptosomes or by a ligand binding assay to measure dopamine transporter function. Prior to MPTP injection, animals were treated with nicotine, or exposed to cigarette smoke or antioxidant compounds.
Results to Date:
Neurotoxic effects of MPTP were observed. Mouse striatal dopamine uptake and the binding of labeled cocaine and mazindol (associated with neuronal uptake of dopamine) were reduced by 50 percent after five injections of MPTP. Pargyline (a monoamine oxidase inhibitor) prevents the lesion. Ascorbic acid (an antioxidant) appreciably prevented reduction of labeled mazindol binding. Acute nicotine or cigarette smoke exposure did not appear to have any effect; however, chronic studies are in progress.

Future Plans:
Additional antioxidant compounds are being tested. Evidence that heavy smokers have a lower incidence of Parkinson's disease and chronically elevated blood levels of carboxyhemoglobin suggest that such a reducing environment could partially protect nigrostriatal neurons from oxidant damage. Cigarette smoke components may be effective at lower levels of neurotoxins.
Project Dates:
July 1984–July 1985.
Financial Support:
CTR.

1252. NATHAN S. KLINE INSTITUTE, CENTER FOR NEUROCHEMISTRY, Ward's Island, New York, New York 10035.

Project Title:
Nicotine Binding Sites in Brain: Effect of Endogenous Material in Brain.

Principal Investigators:
Sershen, H.; Reith, M.E.A.; Lajtha, A.
Objective:
To (1) purify a substance that inhibits (^{3}H)nicotine binding; (2) examine whether inhibitory activity of the partially purified fraction could be abolished by treatment with peptidases or acid hydrolysis; and (3) test whether this endogenous inhibitory material might provide a tool to distinguish binding sites for (^{3}H)nicotine from those for (^{3}H)acetylcholine.
Methods or Approach:
For the binding assay, adult male BALB/cBy mice were decapitated and brain cortices were rapidly removed, homogenized in 0.25 M sucrose, and centrifuged at 1,000 g for 10 minutes. The supernatant was recentrifuged at 35,000 for 10 minutes, and the resulting pellet was washed twice with 50 mmol Tris buffer (pH 7.4). Nicotine binding was measured by previously described method. Portions of the freshly prepared membranes were incubated in triplicate at 21° C for 20 minutes with 12 nmol (±)-(^{3}H)nicotine in presence or absence of 4 mmol nicotine for defining nonspecific binding. Free ligand was separated from membrane-bound (^{3}H)nicotine by filtration and after purification were analyzed for radioactivity. Whole brains from 20 mice were homogenized, purified, and tested for inhibitory activity. One unit of inhibitory activity is defined as amount that inhibits specific binding by 50 percent, as estimated from log probit analysis.
Results to Date:
Supernatant obtained from mouse brain homogenates contains material that inhibits saturable binding of (^{3}H)nicotine in mouse cerebral cortex. Inhibitory material was further purified by heat denaturation, ultrafiltration, and gel chromatography. The material inhibited binding of (^{3})acetylcholine with the same potency as it did that of (^{3})nicotine. It also had some affinity for sites that specifically bind (^{3}HOD-Ala, D-Leu encephalin, but had much lower affinity for binding sites for (^{3}H)quinuclidinyl benzilate, (^{3}H)spiroperidol, (^{3}H)naloxone, or (^{3}H)imipramine. Acid hydrolysis destroyed activity. Preliminary results suggest presence in brain of nicotine-like substances, one of which may be the endogenous ligand for sites that specifically bind (^{3}H)nicotine.
Future Plans:
Search for the endogenous ligand, which may bear a structural resemblance to nicotine, will continue.
Project Dates:
January 1983–December 1984.

Financial Support:
CTR.

1253. NAYLOR DANA INSTITUTE, 1 Dana Road, Valhalla, New York 10595.

Project Title:
Metabolic Epidemiology of Oral Cavity Cancer.

Principal Investigator:
Hecht, S.S.
Objective:
To establish the biochemical basis for the epidemiologic observation that smokers who drink heavily have a higher risk of oral cavity cancer than those who are light drinkers or nondrinkers.
Methods or Approach:
Parallel studies are carried out on carcinogen activation and detoxification in animal model systems and in human tissues. Biopsy samples and exfoliated cells from oral tissues of individuals with known histories of smoking and drinking are used to measure the rates of metabolic activation and detoxification of the tobacco smoke carcinogen benzo(*a*)pyrene (BaP). Results are compared with those of analogous studies using microsomes and cytosol isolated from the cheek pouch epithelium of Syrian golden hamsters treated with ethanol-containing or control liquid diets.
Results to Date:
Chronic alcohol consumption significantly increases the rate of metabolic activation of BaP to its proximate carcinogen 7,8-dihydro-7,8-dihydroxybenzo(*a*)pyrene (BaP-7,8-diol) in hamster cheek pouch epithelial microsomes. Oral tissue microsomes from patients with known histories of alcohol consumption metabolize BaP to several products including BaP-7,8-diol. Chronic alcohol consumption decreases hepatic glutathione levels in hamsters. Measurement of oral glutathione levels in hamsters and humans is in progress.
Future Plans:
Levels of BaP-DNA adducts and of oxidized, reduced, and protein-bound glutathione will be determined in exfoliated cells of individuals with known histories of smoking and drinking.
Project Dates:
September 1982–continuing.

1254. NEW YORK STATE DEPARTMENT OF HEALTH, Corning Tower Building, Empire State Plaza, Albany, New York 12237.

Project Title:
Collaborative Epidemiologic Studies of AIDS: Non-Hodgkins Lymphoma Case Control Study.

Principal Investigator:
Nasca, P.C.
Objective:
To investigate the frequency of AIDS-related risk factors in addition to other risk factors such as smoking in patients with non-Hodgkin's lymphoma residing in upstate New York.
Methods or Approach:
A case–control study of approximately 170 men aged 20 to 54 with non-Hodgkin's lymphoma was designed to search for evidence of risk factors known to be associated with AIDS as well as other potential exposures. Age-matched controls will be selected for each case. Face-to-face interviews (including smoking history) will be conducted.
Results to Date:
Interviews have been completed with 20 cases.

Project Dates:
February 1984–January 1986.
Financial Support:
New York State Department of Health.

1255. NEW YORK STATE DEPARTMENT OF HEALTH, Corning Tower Building, Room 536, Empire State Plaza, Albany, New York 12237.

Project Title:
Missed Opportunities in Cervical Cancer Screening.

Principal Investigator:
Howe, H.H.
Objective:
To assess Pap smear histories by age, education, cervical cancer risk factors (including smoking), medical care utilization, and contraindications for screening.
Methods or Approach:
A systematic sample of female residents, aged 25 to 74, of New York State (excluding New York City) were selected. A self-administered questionnaire was mailed to all potential respondents, and three followups were attempted with nonrespondents.
Results to Date:
Response rate was 72 percent. Of those responding, 30 percent reported currently smoking cigarettes; 57 percent reported they had never smoked cigarettes.
Project Dates:
August 1984–September 1985.
Financial Support:
New York State Department of Health.

1256. NEW YORK STATE DEPARTMENT OF HEALTH, Corning Tower Building, Room 565, Empire State Plaza, Albany, New York 12237.

Project Title:
Epidemiologic Study of Childhood Gliomas.

Principal Investigator:
Nasca, P.C.
Objective:
To determine the importance of various prenatal and childhood environmental exposures in etiology of childhood gliomas, with special emphasis on prenatal and early childhood exposures to drugs, chemicals, radiation, tobacco, immunizations, and animals. Birth characteristics examined included maternal age, parity, and season of birth.
Methods or Approach:
Telephone interviews were used to ascertain epidemiologic data on mothers of 324 childhood glioma patients and 648 matched controls. Demographic, pathologic, and clinical data were also collected from hospital records, utilizing a standard form. Sample size should allow investigation of study variables with respect to the more common histologic subtypes.
Results to Date:
Preliminary screening of data has been completed and basic relationships between disease risk and each lifestyle variable has been examined. Detailed analysis of birth characteristics data has also been conducted. Publication of results is planned for 1986.
Project Dates:
July 1979–December 1982.
Financial Support:
NCI (1R01CA26194).

1257. NEW YORK STATE PSYCHIATRIC INSTITUTE, 722 West 168th Street, New York, New York 10032.

Project Title:
Epidemiology of Early Reproductive Loss.

Principal Investigators:
Kline, J.; Stein, Z.; Susser, M., et al.
Objective:
To examine the relationship between parental characteristics and exposures and adverse reproductive outcomes.
Methods or Approach:
The primary outcomes under study include spontaneous abortion defined by karyotype of the abortus, birth weight, and gestation among live births. Data on parents include obstetric history, smoking and alcohol use, consumption of caffeine-containing beverages, and contraceptive history. A hospital-based epidemiologic and cytogenetic study of spontaneous abortion has identified all women seeking care for spontaneous abortion (cases) at three hospitals; aborted products of conception were karyotyped and all women were interviewed. Controls were recruited from women registering by the 22 week of gestation in the private and public prenatal care facilities of the same hospitals. Women delivering at 28 weeks or later comprise the control group. Cases, defined by karyotype (e.g., chromosomally normal, trisomy, monosomy X) are compared with controls for frequencies of various exposures. The control group also provides a prospectively studied pregnant sample for the study of risk factors for low birth weight and prematurity.
Results to Date:
Smoking during pregnancy is associated with chromosomally normal spontaneous abortion and, as expected, with decreased birth weight among liveborn singletons. Fevers of 100° C or more, as reported by the woman, are associated with spontaneous abortion of chromosomally normal conceptions. The risk of trisomic and chromosomally normal abortions increases with maternal age; risk of monosomy X is inversely related to maternal age.
Future Plans:
Future analyses will focus on the relationships between spontaneous abortion and consumption of coffee, tea, and soft drinks (including colas).
Project Dates:
December 1981–November 1986.
Financial Support:
NICHD (1R01HD15909).

1258. NEW YORK UNIVERSITY MEDICAL CENTER, 550 First Avenue, New York, New York 10016.

Project Title:
Mutagenesis by Metals of Environmental Significance.

Principal Investigators:
Rossman, T.G.; Kneip, I.J.
Objective:
To investigate the genetic toxicology of metals in order to understand the mechanism of action of carcinogenic metals; develop better systems for screening.
Methods or Approach:
Of all carcinogenic metals tested, chromium appears to behave most like an organic carcinogen in that it is mutagenic to bacteria and causes the induction of λ prophage. Its mutagenicity can be demonstrated most easily in the fluctuation test, a liquid mutagenesis assay. To assess the role of DNA repair in chromate mutagenesis, a variety of strains defective in one or

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more DNA repair pathways were compared in the fluctuation test.

Results to Date:

It was found that mutagenesis by chromate is unaffected by the uvrA-dependent excision repair pathway and is also independent of the SOS system. This supports the hypothesis that chromate causes replication errors, perhaps by causing increased infidelity of the DNA polymerase during replication. Arsenic compounds are not mutagenic in any system, whether prokaryotic or eukaryotic; nor do they cause induction of λ prophage. However, arsenite (but not arsenate) does act as a comutagen with UV light in *E. coli*. When a variety of DNA repair-deficient strains were tested in a comutagenesis assay with arsenite, only strains wildtype for DNA repair were positive, suggesting that arsenite acts as a comutagen by inhibiting the excision repair of pyrimidine dimers. At higher concentrations, arsenite also inhibits error-prone SOS repair. The lack of demonstrable tumorigenicity by arsenite, along with data showing a comutagenic action, suggests that arsenite acts as a cocarcinogen rather than as a primary carcinogen.

Future Plans:

The mechanism of comutagenicity of arsenite will be studied by analyzing the types of mutagens with which arsenite acts as a comutagen. In addition, the genetic toxicology of a large group of metal compounds will be examined using the methods established for chromate and arsenite.

Project Dates:

December 1980–continuing.

Financial Support:

NCI (CA 29258; CA 13343; ES 00260).

1259. NEW YORK UNIVERSITY MEDICAL CENTER, 550 First Avenue, New York, New York 10016.

Project Title:

Biochemical Basis of Predisposition to Chronic Obstructive Pulmonary Disease.

Principal Investigator:

Galdston, M.

Objective:

To define biochemical determinants of susceptibility to chronic obstructive pulmonary disease (COPD) by investigating (1) effect of plasma free fatty acid (FFA) bound to elastin on sensitivity of elastin to degradation by polymorphonuclear leukocyte (PMN) elastase and by alpha-2-macroglobulin-bound elastase (α_2M-HLE); and (2) among smokers of similar smoking history and age period, relationship between pulmonary function status and fasting pre- and post-cigarette-smoking molecular and cellular components of blood.

Methods or Approach:

The sodium salt of linoleic acid was used as a model for the effect that an increase in post-smoking plasma FFA may have on activity of HLE and α_2M-HLE toward the synthetic substrate succinyl-trialanyl-p-nitroanilide (SLAPN) and toward bovine neck ligament ^{3}H-elastin and ^{3}H-elastin treated with sodium linoleate (linoleate-^{3}H-elastin). Healthy smokers (50 males, 37 females) ≥ 40 years, who had smoked ≥ 20 pack-years, volunteered for studies that encompassed history, physical examination, current and past smoking patterns, pulmonary function testing, pre- and post-smoking total plasma FFA, unsaturated, polyunsaturated, and saturated FFA; carboxyhemoglobin concentration (HbCO percent), total and differential leukocyte count, serum alpha-1-antitrypsin (α_1Pi) and α_2M concentration, trypsin inhibitory capacity, and neutrophil lysosomal elastase activity. Multiple regression analysis was used to test the joint effects of several of the variables and interactive factors as predictors of pulmonary function status.

Results to Date:

Sodium linoleate inhibited HLE activity toward SLAPN much more effectively than toward ^{3}H-elastin. However, HLE was much more active toward linoleate-^{3}H-elastin than toward ^{3}H-elastin. α_2M-HLE complex activity toward SLAPN was as sensitive to inhibition by sodium linoleate as was HLE. The α_2M-HLE complex was inactive toward ^{3}H-elastin, but the complex pretreated with sodium linoleate had enhanced activity toward ^{3}H-elastin and greater activity toward linoleate-^{3}H-elastin than toward ^{3}H-elastin. Addition of α_1Pi to the reaction mixtures did not alter the enhanced elastolytic activity of the α_2M-HLE complex. Additional studies suggested that sodium linoleate either altered the conformation of elastin, making elastin a better substrate for α_2M-HLE, or altered conformation of α_2M, making elastin more accessible to the active site of HLE bound to α_2M. Among the 87 smokers, 52 (60 percent) had normal pulmonary function tests results (within the 95th percent confidence limit of predicted values for individuals who never smoked), 26 (30 percent) had abnormality only of one or more of the more sensitive tests of small airways function (FEF$_{25}$ and/or $\Delta N_2/L$), and 9 (10 percent) had, in addition to small airways dysfunction, findings consistent with COPD (i.e., FEV$_1$ ≤ 67 percent predicted, increased FRC, and small airways abnormality). Average pulmonary function measurements moved toward abnormal on going from normal to small airways dysfunction in the COPD group. The COPD group was older and had smoked for a greater number of years than the other two groups. Statistical analysis indicated that the following four variables constituted the most useful model for predicting pulmonary function status: age, total FFA post-smoking, polyunsaturated FFA post-smoking times years of smoking, and polyunsaturated FFA post-smoking times α_2M. This model accounted for 13 percent of the variability in pulmonary function status. Because of the relatively small number of subjects, especially those with COPD, analyses are viewed as suggestive and hypothesis-generating, pointing to polyunsaturated FFA as they interact with smoking and other biochemical parameters as potential leads for future research. Comparison of 39 smokers (20 males, 19 females) and 38 healthy nonsmokers (20 males, 18 females; none of the females was pregnant or on contraceptive pills) of the concentration of the serum antioxidants ceruloplasmin (Cp) and transferrin available iron-binding capacity (AIBC) showed that (1) Cp concentration was higher in smokers than in nonsmokers of either sex (more so in females than in males); (2) AIBC concentration did not differ between groups; and (3) antioxidant activity (AOA) per µmol Cp was about 16 times greater than that per µmol AIBC. However, serum AIBC concentration (µmol/L) was about 15 times greater than that of Cp (µmol/L). These serum proteins acted additively, contributing about equally to serum AOA, and together accounted for 60 to 80 percent of serum AOA. For the same physiological concentrations of serum Cp and AIBC, serum AOA was significantly higher (8 percent, $p < 0.01$) in nonsmokers than in smokers. In vitro ceruloplasmin, and also transferrin, prevented suppression of the elastase inhibitory capacity of α_1Pi by cigarette smoke solution and by the oxidant chloramine T. The capacity of serum α_1Pi to inhibit porcine pancreatic elastase was similar in smokers and nonsmokers and unrelated to tar and nicotine content of cigarettes smoked; pre- and post-smoking venous or arterial blood HbCO; or time blood was collected in relation to smoking and level of serum AOA.

Project Dates:

January 1979–December 1981.

Financial Support:
New York University Medical Center; CTR; Louis and Rose Klock Foundation.
References:
(1) Finlay, T.H.; Kadner, S.S.; Nathoo, S.A., et al. "Effects of Detergents on the Activity of α_2-Macroglobulin-Protease Complexes." In: Feinman, R.D. (Editor). *Chemistry and Biology of α_2-Macroglobulin.* Annals of the New York Academy of Sciences, Volume 421, 1983, pp. 340-351. (2) Galdston, M.; Levytska, V.; Schwartz, M.S., et al. "Increased Serum Ceruloplasmin and Impaired Antioxidant Activity in Cigarette Smokers, and Ability to Prevent Suppression of Elastase Inhibitory Capacity of Alpha$_1$-Proteinase Inhibitor." *American Review of Respiratory Disease* 129:258-263, 1984. (3) Galdston, M.; DaCosta, G.; Levytska, V., et al. "Coordinated Antioxidant Activity of Serum Ceruloplasmin and Transferrin-Available Iron Binding Capacity in Smokers and Nonsmokers." *American Review of Respiratory Disease* 129(4): A317, 1984.

1260. NEW YORK UNIVERSITY, SCHOOL OF MEDICINE, 100 Washington Square East, New York, New York 10003.

Project Title:
Regional Deposition of Inhaled Particles in Man.

Principal Investigators:
Lippmann, M.; Albert, R.E.; Schlesinger, R.B., et al.
Objective:
To determine the range of sizes of the bronchial and alveolar airspaces in human lungs; investigate the effects of variations in airspace dimensions on the regional deposition of inhaled particles.
Methods or Approach:
Measurements of the vivo particle deposition will be made, for both cigarette smokers and nonsmokers, with monodisperse aerosols of triphenyl phosphate and ferric oxide, the latter being tagged with 99mTc or 198Au. Concurrently, a series of sequential measurements will be made on the freshly excised lungs of adult smokers, nonsmokers, and children dying accidentally, and on hollow airway casts and tissue sections made from these lungs. Measurements will include respiratory mechanical function, airspace sizes using aerosol probes, bronchial airway morphometry on solid lung casts, intrabronchial deposition patterns in hollow airway casts, and alveolar airspace dimension on lung sections. Similar techniques will be applied in tests performed on donkeys, involving in vivo aerosol deposition, sacrifice, tests of mechanical function and aerosol deposition in their excised lungs, preparation of lung casts and tissue sections, and measurements of particle deposition and airspace sizes. Direct comparisons will be between in vivo airspace sizes and those measured in the casts and sections, and between airspace sizes and particle deposition.
Results to Date:
Results are not yet available.
Future Plans:
The results of all of these tests will be incorporated into predictive deposition models which take anatomic variability into account, including variability associated with age, cigarette smoking, and constitutional factors.
Project Dates:
July 1977–June 1982.
Financial Support:
NIEHS (R01 ES 00881-09).
Reference:
Lippman, M. "Use of Cyclones for Size-Selective Aerosol Sampling." In: Lundgren, D.V.A., et al. (Editors). *Aerosol Measurement.* Gainesville, Florida, University of Florida Presses, 1979, pp. 66-69.

1261. NEW YORK UNIVERSITY, MEDICAL CENTER, 550 First Avenue, New York, New York 10016.

Project Title:
The Pattern of Polonium-210 From Cigarette Smoke on Airway Surfaces in Rats Measured With Etched-Track Detectors.

Principal Investigators:
Cohen, B.S.; Harley, N.H.
Objective:
To measure distribution and clearance of alpha radioactivity in lungs of rats after inhalation of smoke from cigarettes highly enriched in polonium-210 (^{210}Po).
Methods or Approach:
Female Fischer rats were exposed daily for 6 months to smoke from cigarettes with 500 times the normal content of ^{210}Po. Control rats were exposed to standard cigarette smoke. Animals were serially withdrawn and sacrificed. After autopsy, the trachea and major bronchi, larynx, and nasopharynx were examined for surface alpha activity by an etched track technique utilizing cellulose nitrate detectors. Lower lungs were analyzed radiochemically for ^{210}Po.
Results to Date:
Hot spots were seen on samples of larynx from rats exposed to "hot" cigarettes, but no other local accumulations were seen on airways. Both radiochemical analysis and track measurements showed highly elevated activity concentrations in exposed rats. Following withdrawal from smoking, both short- and long-term clearance components were seen. The parameters that fit the clearance data cannot fit the buildup of lung burden. Reduction of surface activity on the airways parallels that of the lower lung during the months following cessation of smoking.
Project Dates:
April 1979–December 1984.
Financial Support:
USDA.

1262. NORTH SHORE UNIVERSITY HOSPITAL, 300 Community Drive, Manhasset, New York 11030.

Project Title:
Maternal Substance Use and Selective Fetal Malnutrition.

Principal Investigators:
Fisher, S.E.; Karl, P.
Objective:
To study the effects of maternal alcohol, tobacco, caffeine, and marijuana use during pregnancy; evaluate the in vitro effect of the major xenobiotics found in the substances.
Methods or Approach:
The effect of each xenobiotic (or combinations) upon critical placental function will be measured in vitro using human placental tissue, including amino acid uptake and transport, folic acid transport, folic acid receptor activity, steroid hormone biotransformation, and (Na,K)-ATPase activity. Human placental slices, placental vesicles, and isolated perfused human placenta will be used. The physiologic and biochemical parameters will also be measured in rat placenta following in vivo xenobiotic exposure. The model permits variation in dosage and gestational timing and correlation with gross teratogenic effects on the rat fetus. Folic acid receptor and (Na,K)-ATPase activities will also be measured in primate placenta, exposed chronically (in vivo) to ethanol. After

bypassing the placenta, xenobiotic effects on fetal organ protein synthesis will be evaluated in rodents. Findings will be of potential importance in the prevention of birth defects and possibly the determination of a margin of safety for substance use during pregnancy.
Results to Date:
Project is in a preliminary phase.
Project Dates:
July 1983–July 1987.
Financial Support:
NIAAA (5K02AA00074-02); NICHD (5R01HD17375-02).

1263. PROCESS AND INSTRUMENTS CORPORATION, 1943 Broadway, Brooklyn, New York 11207.

Project Title:
A Second Generation Automatic, Programmable, Continuous Cigarette Smoking and Animal "Inhaled-Smoke" Exposure System for Large Numbers of Animals.

Principal Investigator:
Greenspan, J.
Objective:
To redesign and simplify the SEM-II system to produce a relatively low cost, flexible system for programmed production and distribution of cigarette smoke and other aerosols to only the snouts of large numbers of animals.
Methods or Approach:
Simplicity, flexibility, and reasonable cost will be attained by (1) use of recently developed, commercially available solid state programmable controllers; (2) modular construction of function elements of the system; (3) improvements in various mechanical and instrumentation components of the smoke production and distribution system; and (4) further development of the animal containment system and its monitoring and failsafe controls.
Results to Date:
A number of system design features have been developed and incorporated into an operational prototype unit.
Future Plans:
Plans include manufacturing and supply of systems commercially to research projects that require such system capabilities.
Project Dates:
October 1977–December 1985.
Financial Support:
Process and Instruments Corp.

1264. PROCESS AND INSTRUMENTS CORPORATION, 1943 Broadway, Brooklyn, New York 11207.

Project Title:
An Automatic, Continuous Aerosol Generating and "Snout-Only" Aerosol Exposure System for Large Numbers of Animals.

Principal Investigator:
Greenspan, J.
Objective:
To design, develop, and construct an automatic, continuous aerosol generating and "snout-only" aerosol exposure system for large numbers of animals.
Methods or Approach:
Research will include investigation of methods and combinations of methods for continuous generation of aerosols in the 0.1 to 1.0 micron range from solid, vapor, or solution phases; investigation of methods for mixing aerosols with other components or aerosols, such as cigarette smoke; adaptation of aerosol generators to a programmed distribution system; and coupling of the above systems with previously developed animal containment systems.
Results to Date:
Ongoing investigations have resulted in development of aerosol generators and a study of their characteristics.
Future Plans:
Inhalation studies will be conducted on a wide variety of aerosols and aerosol admixtures.
Project Dates:
November 1977–1986.
Financial Support:
Process and Instruments Corp.

1265. RESEARCH INSTITUTE ON ALCOHOLISM, 1021 Main Street, Buffalo, New York 14203.

Project Title:
Stress, Race and Alcohol Use in a Household Population.

Principal Investigators:
Russell, M.; Welte, J.W.
Objective:
To study interactions between stress-producing life events, stress modifiers, and stress manifestations in black and white household populations; determine relative contributions of stress manifestations (anxiety, smoking, diet, alcohol use) to high blood pressure, particularly among blacks.
Methods or Approach:
Drinking patterns; various elements of stress producers, modifiers, and manifestations; blood pressure; weight and height; and smoking patterns will be measured in a representative household sample of 1,000 whites and 1,000 blacks, stratified by socioeconomic status. Relationships of interest will be described; interaction models will be tested by path analyses.
Results to Date:
Project is in a preliminary phase.
Future Plans:
Data will be used to develop intervention programs for problem drinking, particularly among blacks.
Project Dates:
January 1985–December 1987.
Financial Support:
NIAAA (1R01AA05702-01A2).

1266. RESEARCH INSTITUTE ON ALCOHOLISM, 1021 Main Street, Buffalo, New York 14203.

Project Title:
Maternal Alcohol Use and Pregnancy Outcome.

Principal Investigators:
Russell, M.; Cowan, R.
Objective:
To elucidate fetal effects of maternal alcohol and other drug use.
Methods or Approach:
At a prenatal care visit, 567 obstetric patients completed a self-administered questionnaire on drinking patterns prior to pregnancy, alcohol-related problems, smoking, and other drug use. Medical records for prenatal care, delivery, and newborn status were reviewed for pregnancy outcome measures.
Results to Date:
Smoking, but not drinking prior to pregnancy, was found to be significantly related to intrauterine growth. Depressed newborn status, measured by lower Apgar scores, was related to symptoms of problem drinking, but not smoking, alcohol intake prior to pregnancy, or other drug use.

Future Plans:
Followup of intelligence quotient, visual motor integration, hyperactivity, and dichotic listening will be conducted on children at 6 years of age.
Project Dates:
June 1978–June 1986.
Financial Support:
NIAAA (1R01AA06437-01); ew York State Health Research Council (11-015); Research Institute on Alcoholism.

1267. ROSWELL PARK MEMORIAL INSTITUTE, 666 Elm Street, Buffalo, New York 14263.

Project Title:
Cancer Control By Self-Help Stop Smoking Interventions.

Principal Investigator:
Cummings, K.M.
Objective:
To demonstrate feasibility of using a telephone hotline to disseminate information to smokers on how to quit smoking; evaluate relative effectiveness of alternative self-help smoking cessation manuals in helping smokers quit.
Methods or Approach:
An experimental design is being used to compare the effectiveness of five alternative self-help smoking cessation booklets. Four have been varied on a combination of two variables: (1) instruction on how to quit smoking (cold turkey or gradual reduction); and (2) the structure of the manual (either day-to-day instructions or the same instruction not given in day-to-day format). The four social learning oriented self-help booklets include preparation for quitting, cessation, and maintenance of cessation. In addition, a fifth control manual is being evaluated that provides general information on smoking and smoking cessation, but does not give specific suggestions on how to quit. The planned study population will include approximately 2,000 adult smokers who call the stop smoking hotline at the institute to request information of how to quit smoking. Eligible subjects will be followed up by telephone at 1- and 6-month intervals following enrollment, to assess usage of the booklet and to document changes in smoking status.
Results to Date:
The stop-smoking hotline was started in August 1984. The five self-help booklets have been written and pretested for readability (set at eighth grade level).
Project Dates:
February 1984–January 1986.
Financial Support:
NIH (CA 36265-02).

1268. ROSWELL PARK MEMORIAL INSTITUTE, 666 Elm Street, Buffalo, New York 14263.

Project Title:
Evaluation of a Training Program to Teach Physicians Counseling Methods to Aid Smokers in Quitting.

Principal Investigators:
Cummings, K.M.; Giovino, G.; Sciandra, R.
Objective:
To evaluate the impact of a 2-hour training program designed to teach physicians counseling strategies to aid smokers in quitting.
Methods or Approach:
A pretest–posttest control group design was employed to evaluate impact of the training program among 28 residents in family practice working at a family medicine clinic in Buffalo; 10 were exposed to training and the remaining 18 attended a lecture on a topic not related to smoking cessation. A questionnaire assessing attitudes about smoking and smoking cessation and antismoking counseling practices was administered 2 weeks before and again 4 months after training. The patient population included adult cigarette smokers who visited one of the study physicians during the 3.5-month period following training. Patients were questioned about current and past smoking habits. Telephone interviews were conducted with patients 3 months after enrollment to assess changes in smoking practices and about antismoking advice received from physicians during the preceding 3 months.
Results to Date:
Physicians who attended training were more likely to (1) advise patients who smoked to set a target date for quitting, (2) forewarn patients about withdrawal symptoms, (3) provide self-help booklets, (4) refer patients to stop smoking clinics, and (5) schedule followup visits to monitor cessation progress. Training program participants also reported feeling better prepared to counsel patients. The program also had a small, but consistent, effect on patient smoking behavior; those who saw physicians from the training program were more likely to report having made an attempt to quit smoking, to have made a serious attempt to quit, and to have quit. The 3-month quit rate among patients of trained physicians was 37 percent higher than the quit rate for patients of physicians in the control group (9.5 vs. 6.9 percent).
Future Plans:
The effect of specific physician counseling practices and characteristics of patients (i.e., sex, age, health status) most affected by physicians' counseling will be studied.
Project Dates:
January 1984–December 1985.
Financial Support:
NCI (PO 263MD427932, P30CA16056-10S).

1269. ROSWELL PARK MEMORIAL INSTITUTE, 666 Elm Street, Buffalo, New York 14263.

Project Title:
Patient Epidemiology Data System (PEDS).

Principal Investigator:
Mettlin, C.
Objective:
To establish a data base to carry out case–control and other studies on factors of possibly etiological significance in cancer.
Methods or Approach:
Approximately 4,000 new cancer patients enter the institute annually, and on admission, all patients, excluding prisoners, pregnant women, and minors, complete a 16-page questionnaire. Data obtained concern (1) demographic characteristics, (2) smoking history, (3) alcohol use, (4) residential history, (5) occupational history, (6) health history, (7) food frequency history, (8) chemical medication, radiation, sunlight exposures, and (9) family history. Data on smoking are obtained routinely for use as primary study variables or for controlling confounding in other investigations. Multiple cancers are under investigation, including those typically associated with tobacco use, such as oral cancer, respiratory cancers, bladder cancers, and others. The interaction of risk factors, particularly family history of cancer, is also under investigation. Patients in the hospital are followed with a volunteer visit and after discharge by mail and telephone followup to insure completeness of response and to assess accuracy of data. Comparable information is being obtained from clients of the Roswell Park Prevention/Detection Center as one source of control patients.

Data are coded and entered on a computer for subsequent analysis using case–control analytic techniques.

Results to Date:

Preliminary data (2 years of the 5-year study have been completed) show that response rates are largely a function of the seriousness of the cancer diagnosis and the expected survival of the patient on admission. Short-term survivors are least likely to complete the questionnaire. Stage at diagnosis, age, and diagnosis with respiratory disease are also predictors of response status.

Future Plans:

When sufficient data are available, multivariant analyses of cancer etiology involving tobacco use and other factors will be conducted.

Project Dates:

September 1983–continuing.

Financial Support:

ACS (SIG-12).

1270. SMITH BARNEY HARRIS UPHAM CO., INC., 1345 Avenue of the Americas, New York, New York 07030.

Project Title:

Tobacco Monitor.

Principal Investigators:

Morrow, R.; Yacullo, M.A.

Objective:

To analyze key variables of the tobacco industry from an investment standpoint; examine trends, government regulations, sales, costs, consumption, and smoking and health issues.

Methods or Approach:

Every 3 months, significant information is gathered from various sources (trade magazines, government agencies) and statistics are calculated and compiled.

Results to Date:

Each variable is examined and analyzed, and projections are made of the industry and major tobacco companies. The positive and negative effects of issues facing the industry and manufacturers, such as health and taxes, are reported. Also reviewed are what tobacco companies are doing to counteract the negative aspects, what groups are doing to oppose smoking of tobacco products, and reactions of the Government.

Project Dates:

September 1980–continuing.

Financial Support:

Smith Barney Harris Upham Co., Inc.

1271. ST. MARY'S HOSPITAL, 89 Genesee Street, Rochester, New York 14611. HIGHLAND HOSPITAL, South and Bellevue Roads, Rochester, New York 14620.

Project Title:

The Effects of Smoking Cessation on Airway Reactivity.

Principal Investigators:

Israel, R.H.; Ossip-Klein, D.J.; Poe, R.

Objective:

To determine airway reactivity in a group of symptomatic smokers; assess effect of smoking cessation on this response.

Methods or Approach:

Adult symptomatic smokers are assessed before smoking cessation and at 2- and 6-months postcessation, using spirometry, airway reactivity studies (carbachol challenge), and respiratory symptoms questionnaire. Self-reported smoking cessation is validated by alveolar carbon monoxide levels at each testing session.

Results to Date:

Preliminary results suggest no overall improvement in airway reactivity at 2-months postcessation and a significant increase ($p < 0.05$) in reactivity at 6-months postcessation.

Future Plans:

A comparison group of symptomatic continuing smokers is being assessed at identical followup intervals. Similar measures of airway reactivity in children of smokers will be conducted (using a cold air challenge).

Project Dates:

October 1983–continuing.

1272. STATE UNIVERSITY OF NEW YORK AT BUFFALO, SCHOOL OF MEDICINE, 140 Farber Hall, Main and Bailey Avenue, Buffalo, New York 14214.

Project Title:

Self-Initiated Smoking Cessation in College Students.

Principal Investigators:

Hellman, R.; O'Shea, R.M.; Schimpfhauser, F.T., et al.

Objective:

To study the smoking cessation behaviors of college students to determine elements important in successful self-initiated cessation.

Methods or Approach:

A convenience sample of college students awaiting treatment at the outpatient department of a university health service were evaluated; all were between the ages of 17 and 24 and had either quit or had attempted to quit smoking. The 72 participants were interviewed using two versions of the interview instrument, one for quitters and one for recidivists (differences were mostly in phraseology).

Results to Date:

There were many similarities between the 40 successful quitters and the 32 recidivists; differences seemed related to techniques used to remain abstinent, expectations of ease or difficulties in quitting, and the influence of a boyfriend/girlfriend. The differences should be studied in a larger sample to examine the influence of the health service and physician, to identify differences in attitudes toward cessation between quitters and recidivists, and to evaluate what use smokers make of the knowledge gained through previous cessation attempts.

1273. STATE UNIVERSITY OF NEW YORK AT BUFFALO, Department of Social and Preventive Medicine, 2211 Main Street, Buffalo, New York 14214-2699.

Project Title:

Prospective Study of Cancer Epidemiology.

Principal Investigators:

Graham, S.; Marshall, J.; Haughey, B., et al.

Objective:

To study the incidence of cancer at various sites using a prospective design on a large population.

Methods or Approach:

A short questionnaire concerning dietary habits, vitamin use, and smoking and alcohol history was mailed to a random sample of New York State residents who had maintained their current address or telephone number for 18 years or longer. Status of the 58,000 respondents will be followed regarding cancer incidence by means of reports sent to the New York State Tumor Registry. Of interest will be various facets of diet and the relationship between the incidence of cancer and

ingestion of meats, fats, cruciferous vegetables, fiber, vitamins A, C, and E, coffee, and alcohol. The interaction between dietary parameters and other risk factors (including tobacco use) will be investigated; e.g., whether the finding that vitamin A is associated with a reduction in risk among heavy and light smokers will be upheld in a prospective design.
Results to Date:
Results are not yet available.
Future Plans:
Followup of subjects will continue through 1985; final analyses will be initiated when 5-year followup is completed.
Project Dates:
April 1980–July 1985.
Financial Support:
NCI (CA11535).

1274. STATE UNIVERSITY OF NEW YORK AT BUFFALO, 2211 Main Street, Buffalo, New York 14214.

Project Title:
Epidemiology of Oral Cancer.

Principal Investigators:
Graham, S.; Frischman, S.L.; Kaufman, S., et al.
Objective:
To determine the various nutritional and and other factors common to patients with cancer of the oral cavity.
Methods or Approach:
Self-administered questionnaires and interviews were used to obtain data from oral cancer patients on oral hygiene, use of dental prostheses, smoking, and alcohol consumption in addition to dietary information.
Results to Date:
Project was completed and results have been published.
Reference:
Marshall, J.; Graham, S.; Mettlin, C., et al. "Diet in the Epidemiology of Oral Cancer." *Nutrition and Cancer* 3:145-149, 1982.

1275. STATE UNIVERSITY OF NEW YORK AT BUFFALO, Department of Social and Preventive Medicine, 2211 Main Street, Buffalo, New York 14214.

Project Title:
Tri-County Study of Cancer of the Gastrointestinal Tract, Lung, and Bladder.

Principal Investigators:
Graham, S.; Marshall, J.; Byers, T., et al.
Objective:
To investigate the epidemiology of cancers at various sites; study the possible relationship between dietary factors and cancer of the gastrointestinal tract, lung, and bladder.
Methods or Approach:
Patients in Erie, Niagara, and Monroe Counties in New York who develop histologically confirmed gastrointestinal, lung, or bladder cancer are interviewed. Major emphasis is on dietary habits (time and frequency of meals, types and amounts of food eaten, and methods of food storage and preparation). Questions are also asked about alcohol consumption, tobacco use, use of certain drugs, and illness history. Data on age, occupation, and marital status are also gathered. Neighborhood controls matched for age (±5 years) and sex are also interviewed.
Results to Date:
Results are not yet available.
Project Dates:
January 1975–July 1985.
Financial Support:
NCI (CA11535).

1276. STATE UNIVERSITY OF NEW YORK AT BUFFALO, 2211 Main Street, Buffalo, New York 14214.

Project Title:
Upstate New York Diet Study: Case–Control Study of Lung Cancer.

Principal Investigators:
Graham, S.; Byers, T.; Marshall, J., et al.
Objective:
To investigate dietary and nondietary etiologic factors in lung cancer.
Methods or Approach:
The study cohort consists of lung cancer cases among white males and females in three western counties in New York State diagnosed between 1979 and 1984 (304 males, 154 females) and controls matched for neighborhood (724 males and 404 females selected as controls for other parallel cancer studies). Interviews are conducted in the home to collect data on diet and a variety of other environmental risk factors.
Results to Date:
A negative correlation was found between consumption of foods containing carotene and lung cancer and all histologic subtypes of lung cancer in both men and women. No association was found for fat, calories, vitamins C and E, fibre, protein, or retinol. The protective effect of carotene was independent of age, sex, and cigarette smoking.
Future Plans:
Additional analyses will be conducted on the interaction between tobacco and carotene. Occupational exposures will be also be analyzed, as will the relationship between lung cancer and the use of pipes, cigars, and other forms of tobacco.
Project Dates:
1979–1985.
Financial Support:
NCI (CA11535).

1277. STATE UNIVERSITY OF NEW YORK, STONY BROOK, Department of Psychology, Stony Brook, New York 11794.

Project Title:
Life Stress and Coronary Risk Factors (Including Smoking) in Families.

Principal Investigator:
Weidner, G.
Objective:
To (1) determine whether behavioral and physiological coronary risk factors aggregate in families and cluster in individuals; (2) examine relationship of type A behavior and life stress to smoking, lack of exercise, and physiological risk factors; and (3) investigate the relationship of stress, smoking, and coffee drinking to physiological risk factors.
Methods or Approach:
Physiological coronary disease risk factors investigated will include elevated levels of plasma cholesterol and systolic and diastolic blood pressure. Analysis will be based on behavioral and physiological data from 403 free-living families who will be followed for 5 years.
Results to Date:
Project is in a preliminary phase.
Project Dates:
September 1984–August 1937.

Financial Support:
NHLBI (1R23HL34261-01).

1278. STATE UNIVERSITY OF NEW YORK, Department of Economics, and Community and Preventive Medicine, Stony Brook, New York 11790. AMERICAN HEALTH FOUNDATION, 320 East 43rd Street, New York, New York 10077.

Project Title:
Smoking Impact on Mortality and Morbidity: Allocation in Multiple Risk Situations, Particularly Workplaces.

Principal Investigator:
Kristein, M.M.

Objective:
To review the association between cigarette smoking and mortality and the relationship between per capita cigarette smoking and mortality rates for heart disease and respiratory cancer for the period 1940 to 1979 in the United States.

Methods or Approach:
Econometric and statistical methods were used to evaluate epidemiological and clinical data for the period studied.

Results to Date:
Findings suggest a 20-year lag relationship between smoking (especially number of cigarettes consumed per capita) and respiratory cancer mortality, although there appears to be no lag in the relationship of smoking (especially pounds of tobacco consumed per capita) with heart disease mortality. Smoking was found to explain over 90 percent of the variance in the relationship between smoking and respiratory cancer mortality, while explaining only 50 percent of the variance between smoking and heart disease mortality. Nonsmoking asbestos workers have 5 times the mortality risk from lung cancer as do nonsmoking, nonasbestos workers; however, smokers, whether asbestos workers or not, have 11 times the lung cancer mortality rate as nonsmokers.

Financial Support:
University of New York, Stony Brook; American Health Foundation.

Reference:
Kristein, M.M. "40 Years of U.S. Cigarette Smoking and Heart Disease and Cancer Mortality Rates." *Journal of Chronic Diseases* 37(5):317-323, 1984.

1279. STATE UNIVERSITY OF NEW YORK, Department of Economics, and Community and Preventive Medicine, Stony Brook, New York 11790. AMERICAN HEALTH FOUNDATION, 320 East 43rd Street, New York, New York 10077.

Project Title:
Cost of Smoking to Business and Possible Savings Due To Business Policies to Reduce Smoking in Workplaces.

Principal Investigator:
Kristein, M.M.

Objective:
To study the costs of employing workers who smoke in various types of workplaces; determine effect of workplace policies against smoking.

Methods or Approach:
Economic and epidemiologic data from various sources were evaluated to determine smoking-related costs.

Results to Date:
Smoking-related business costs (including long-range costs such as absenteeism, premature mortality, and illness) may be as high as 1,000 dollars/year for each smoker. A policy of no smoking plus a policy of hiring nonsmokers comes under a company's right to define the nature of the workplace and the appropriate behavior of its employees while at work, a right that has been upheld in most legal contexts. While such a program will probably cost between 5 and 10 dollars per employee, the employer stands to get a high rate of return on the investment; i.e., a company with 1,000 employees that spent 10,000 dollars to introduce a no smoking policy could save up to 90,000 dollars/year. The excess medical costs to the country of smoking is estimated at 24 billion dollars/year and the loss in GNP is 36 billion dollars/year. The strongest argument against no smoking policies is that the net gains derived are more than offset by the costs of an increase in the numbers of older persons (potential retirees) due to the reduction in premature mortality.

Financial Support:
University of New York, Stony Brook; American Health Foundation.

References:
Kristein, M.M. "Wanted: Smoking Policies for the Work Place." *Business and Health*. pp.14-17, November 1984. (2) Kristein, M.M. "How Much Can Business Expect to Profit From Smoking Cessation?" *Preventive Medicine* 12:358-381, 1983.

1280. STATE UNIVERSITY OF NEW YORK, SCHOOL OF MEDICINE, Stony Brook, New York 11794.

Project Title:
Effect of Cigarette Smoke on Activity of Macrophage Transglutaminase.

Principal Investigators:
Roth, W.; Chung, S.I.; Janoff, A.

Objective:
To test for inhibition of alveolar macrophage (Mφ) transglutaminase (TG) by smoke; examine possible correlations between Mφ TG inhibition and decreased Mφ endolytic function and bactericidal function.

Methods or Approach:
Mφ TG has been implicated in receptor-mediated endocytosis. Alveolar Mφ endolytic function is depressed by cigarette smoking, which may partly explain smokers' increased susceptibility to airway infection. It has previously been shown that smoke inhibits activity of plasma transglutaminase (Factor XIIIa). Methodology will be to (1) purify rabbit alveolar Mφ TG; (2) conduct dose–response study of smoke effect on pure Mφ TG activity (assay method will incorporate ^{14}C-putrescine into casein in the presence of enzyme); (3) study chemical mechanism of TG inactivation by smoke; (4) measure endocytosis, bactericidal activity, and TG activity of cultured rabbit alveolar Mφ after incubation with/without cigarette smoke; and (5) measure activity of TG in lysates of alveolar Mφ harvested from human smokers and nonsmokers.

Results to Date:
Rabbit alveolar Mφ TG has been purified and enzyme inactivation by smoke (by oxidation) has been demonstrated. Dithiothreitol protects TG against inactivation by smoke. Results from studies in progress are not yet available.

Project Dates:
September 1982–December 1985.

Financial Support:
NHLBI (HL 14262); NIEHS (5T32ES07088).

1281. STATE UNIVERSITY OF NEW YORK, SCHOOL OF MEDICINE, Stony Brook, New York 11794.

Project Title:
In Vitro Activation of the Alternative Pathway of Complement by Cigarette Smoke.

Principal Investigators:
Kew, R.; Ghebrehiwet, B.; Janoff, A.

Objective:
To test the possibility that components of cigarette smoke can activate the complement system and generate complement-derived chemotactic peptides.

Methods or Approach:
In vitro methods include (1) measurement of serum hemolytic activity after incubation with buffer (negative control), methylamine (a known activator of C3, positive control), or cigarette smoke; (2) measurement of MG-EGTA-treated serum hemolytic activity after addition of purified C3 that was previously treated with buffer, methylamine (CH_3NH_2), or smoke; (3) titration of C1 γ and C4 in smoke-treated serum; (4) binding assays for factors H and I, using buffer-treated, CH_3NH_2-treated, and smoke-treated C3; and (5) measurement of ^{125}I-iodoacetamide and ^{14}C-CH_3NH_2 uptake by purified C3; treated as in (4).

Results to Date:
Smoke, like CH_3NH_2, depletes serum hemolytic activity. Pure C3, treated with smoke or CH_3NH_2 and added to Mg^{+}-EGTA-treated serum (to block the classical pathway of complement), causes loss of hemolytic activity by alternative pathway activation. C1 γ is not activated by incubation of serum with smoke; however, C4 is affected. Smoke-treated C3 binds less factor H and less factor I than CH_3NH_2-treated C3. CH_3NH_2-treated C3 subsequently binds 1 mole of ^{125}iodoacetamide/mole and <0.1 mole CH_3NH_2/mole, while smoke-treated C3 appears not to bind ^{125}iodoacetamide and binds approximately 1.0 mole $^{14}CH_3NH_2$/mole, suggesting that smoke activates C3 by a mechanism independent of thiolester cleavage.

Future Plans:
Further studies will (1) determine chemical mechanism of C3 activation by smoke; (2) measure levels of chemotactic complement peptides in lung secretions from smokers and nonsmokers; and (3) measure chemotactic activity of lung secretions in smoke-exposed experimental animals (intact or depleted of C3 by treatment with cobra venom factor or genetically deficient in C5).

Project Dates:
July 1982–August 1985.

Financial Support:
NHLBI (HL 14262); NIEHS (5T32ES07088).

1282. STATE UNIVERSITY OF NEW YORK, BUFFALO, SCHOOL OF DENTISTRY, Buffalo, New York 14214.

Project Title:
Oral Cancer in Israel.

Principal Investigators:
Fischman, S.L., Ulmansky, M.; Gazit, D.

Objective:
To (1) correlate the incidence of smoking and alcoholism with the incidence of oral cancer in Israel; (2) compare the incidence of oral cancer in Israel with oral cancer in the United States; and (3) review premalignant conditions of the oral cavity in Israel.

Methods or Approach:
All cases of oral cancer and of premalignant conditions in Israel are being reviewed. Histologic and clinical data are being recorded.

Results to Date:
Data on oral cancer in Israel revealed a lower incidence and later onset age than in other countries. It was also noted that there was a high prevalence of smoking and a low incidence of alcoholism in Israel. Results have been published.

Project Dates:
April 1981–1985.

Financial Support:
Lady Davis Fellowship, Jerusalem.

Reference:
Gazit, D.; Ulmansky, M.; Fischman, S., et al. "A Study of a Sample of Oral Cancer in Israel." *Oral Surgery, Oral Medicine, Oral Pathology* 57(1):118-121, January 1984.

1283. STATE UNIVERSITY OF NEW YORK, BUFFALO, Department of Social and Preventive Medicine, 2211 Main Street, Buffalo, New York 14214.

Project Title:
Physician Influence on Smoking Cessation of College Students: A Minimal Intervention.

Principal Investigators:
Hellman, R.; O'Shea, R.M.; Schimpfhauser, F.T., et al.

Objective:
To evaluate a smoking cessation strategy of minimal intervention by student health physicians in a college population.

Methods or Approach:
A quasi-experimental design was used. The convenience sample of college students, all current smokers, attended a University Health Service and were seen by a health service physician. The 179 controls were chosen first, and after filling out a baseline questionnaire about smoking, proceeded through the health service in the routine manner. Before selecting the experimental group, physicians were given orientation on the study and on their responsibilities. The 171 students in the experimental group filled out the baseline questionnaire and were given a 3- to 5-minute speech about the hazards of smoking and two booklets from the National Cancer Institute; one assessed reasons for smoking and the other offered suggestions on how to quit. Students were contacted at intervals of approximately 1 month and 6 months following the physician visit, to assess current smoking status.

Results to Date:
Preliminary analysis demonstrates smoking cessation in the predicted direction of an increased quit rate for the experimental group, but the difference between the groups does not reach statistical significance.

Project Dates:
February 1983–November 1984.

Financial Support:
ALA of Western New York Inc.

1284. UNIVERSITY OF ROCHESTER MEDICAL CENTER, CENTER FOR BRAIN RESEARCH, Rochester, New York 14642.

Project Title:
Nicotine Disposition in Hepatocytes.

Principal Investigator:
Abood, L.G.

Objective:
To examine transport mechanisms involved in nicotine uptake and metabolism by rat liver cells.

Methods or Approach:
Binding of ^{3}H-nicotine to rat hepatocytes is measured and the relationship of such binding to metabolism is investigated.
Results to Date:
A saturable, reversible, nonstereoselective binding site for ^{3}H-nicotine has been found in membranes of isolated hepatocytes. The system appears to be related to metabolism of nicotine to cotinine.
Future Plans:
Studies will isolate and further characterize the binding site.
Project Dates:
December 1984–November 1985.
Financial Support:
CTR.

1285. UNIVERSITY OF ROCHESTER MEDICAL CENTER, CENTER FOR BRAIN RESEARCH, 500 Joseph C. Wilson Boulevard, Rochester, New York 14627.

Project Title:
Studies of Nicotine Interaction With Blood Cells.

Principal Investigator:
Hoss, W.P.
Objective:
To identify at the molecular level the effects of nicotine on blood leukocytes and platelets.
Methods or Approach:
Methods used include (1) receptor-binding assays utilizing radiolabeled nicotine; (2) electron-spin resonance (ESR) measurements using spin probes; (3) spectrophotometric monitoring of superoxide ion production; (4) fluorometric monitoring of hydrogen peroxide production; and (5) measurement of granulocyte chemotaxis under agarose.
Results to Date:
A new noncholinergic receptor for nicotine has been identified on human phagocytic leukocytes, lymphocytes, and platelets. The receptor binds nicotine at concentrations present in blood after smoking. Nicotine produces a perturbation in granulocyte membranes as monitored by ESR spectroscopy of a spin probe, and modulates granulocyte chemotaxis.
Future Plans:
The second messenger system mediating the cellular response to nicotine will be identified.
Project Dates:
January 1983–July 1985.
Financial Support:
CTR.

1286. UNIVERSITY OF ROCHESTER, CENTER FOR BRAIN RESEARCH, Box 605, Rochester, New York 14642.

Project Title:
Isolation and Characterization of the Nicotinic Receptor From Rat Brain.

Principal Investigator:
Abood, L.G.
Objective:
To isolate and purify nicotine receptor from rat brain.
Methods or Approach:
Methods used will include (1) affinity chromatography to purify receptor from triton-solubilized extracts of rat brain membrane; (2) affinity ligands to label receptor in vivo and in vitro; (3) examination of various receptor subtypes using (+)- and (-)- ^{3}H-nicotine; and (4) neuroanatomical localization of receptors in rat brain, particularly in brain stem area.
Results to Date:
A 56,000 Mw protein has been purified that appears to be the recognition site for nicotine. The primary sites for nicotine's action in the brain appear to be in the vestibular nucleus and adjacent brain stem areas.
Future Plans:
Further projects will include preparation of monoclonal antibodies to nicotine receptors and localization of vestibular neurons responsible for nicotine-induced prostration.
Project Dates:
February 1980–January 1986.
Financial Support:
NIDA (DA 00464).

1287. UNIVERSITY OF ROCHESTER, SCHOOL OF MEDICINE, Departments of Pediatrics and Medicine, 601 Elmwood Avenue, Rochester, New York 14642.

Project Title:
Long-Term Prospective Study in Children After Respiratory Syncytial Virus Infection.

Principal Investigators:
Hall, C.B.; Hall, W.J.; Gala, C.L., et al.
Objective:
To determine whether children hospitalized as infants with respiratory syncytial virus (RSV) have a greater prevalence than controls of allergic diathesis, documented family atopy, or exposure to environmental pollutants; to determine if these predisposing factors or the severity of initial RSV illness might be predictive of subsequent clinical or functional lung abnormalities.
Methods or Approach:
The study was in conjunction with an ongoing community surveillance program that monitors patterns of acute respiratory illness in clinics and private pediatric offices throughout Monroe County, New York. A prospective evaluation was conducted for 8 years of 29 children who were hospitalized during infancy with acute lower respiratory tract illness cause by RSV.
Results to Date:
No differences in prevalence of a family history of atopy or breastfeeding were noted between RSV infants and controls; however, a history of parental smoking was significantly associated with hospital admission for RSV lower respiratory tract disease. Evidence of atopy, defined by serum immunoglobulin E levels and radioallergosorbent testing, have developed in only three (10 percent) of the children. Six children (21 percent) continue to have recurrent lower respiratory tract disease; 55 percent of these children had abnormally low oxyhemoglobin levels (SaO_2), measured by ear oximetry, for the first 3 to 4 years after acute illness; 21 percent have persistently low SaO_2 levels during the eighth year of followup. Spirometric values indicate evidence of peripheral airway obstruction. Results suggest that an association between RSV lower respiratory tract infections and chronic abnormalities of pulmonary function may be detected sequentially through the first 8 years of life. The abnormalities are not limited to those children developing an atopic state during the same time period.
Financial Support:
CTR; USPHS (5PSO AL15372-05).
Reference:
Hall, C.B.; Hall, W.J.; Gala, C.L., et al. "Long-Term Prospec-

tive Study in Children After Respiratory Syncytial Virus Infection." *Journal of Pediatrics* 105(3):358-364, September 1984.

1288. UNIVERSITY OF ROCHESTER, SCHOOL OF MEDICINE AND DENTISTRY, Department of Obstetrics/Gynecology, Box 668, 601 Elmwood Avenue, Rochester, New York 14642.

Project Title:
Placental Toxicology.

Principal Investigators:
Miller, R.K.; Maulik, D.; Di Sant'Agnese, P.A., et al.
Objective:
To develop an in vitro human-rodent placental model to investigate normal function; determine pharmacokinetics and toxicity of environmental agents (e.g., heavy metals and cigarette smoke) without risk to mother or fetus.
Methods or Approach:
Cadmium has been selected as the specific agent for evaluation since it is an environmental pollutant, especially in cigarette smoke. Previous studies have demonstrated that cadmium can be concentrated in the placenta of smokers and that in rodents, cadmium can induce placental necrosis leading to death of the conceptus. Investigations under development will determine how sensitive the human placenta may be to cadmium exposure. An in vitro dual perfused human placental lobule preparation was developed to study normal function and toxicologic response for periods up to 12 hours. Every 4 hours, recirculating maternal and fetal perfusates are totally exchanged. During perfusion, hormone synthesis and release, amino acid transport, pH, glucose, blood pressure and flow rate, blood flow distribution, mitochondrial calcium levels, and ultrastructure are evaluated. The pharmacokinetics of chemicals and effects of these substances on above parameters can be measured in a dose-related manner. The human placenta is obtained immediately at delivery and perfusion of the fetal vasculature and maternal lacunae are established (mother and infant are not exposed to any substances). The technique can also be applied to the study of placentae from patients who have been exposed to environmental agents, e.g., tobacco smoke, therapeutic agents, or other disease processes.
Results to Date:
Research is targeted at the adaptability of the trophoblast to environmental exposure, whether in man or in animals, as reflected in morphological, biochemical, and physiological responses. Dose-related alterations in morphology and biochemistry were noted following cadmium exposure. When the effects of cadmium administered in the maternal perfusate were compared with animal studies, blood levels that would produce placental toxicity in animals without affecting the kidney or liver, were comparable to concentrations noted in maternal perfusate. There appears to be substantial similarity between the rodent and the human in terms of responsiveness to cadmium toxicity.
Future Plans:
Cadmium studies will evaluate metallothionein and the degree to which cadmium can produce its toxicity in the human. To explore the question of chronic toxicity, placentae from smoking mothers will be evaluated.
Project Dates:
December 1982–December 1987.
Financial Support:
NIEHS (R01ES02774).

1289. UNIVERSITY OF ROCHESTER, Department of Psychology, River Station, Rochester, New York 14627.

Project Title:
Self Help Strategies in Long Term Smoking Cessation.

Principal Investigator:
Ossip-Klein, D.J.
Objective:
To (1) evaluate role of community-based smoking relapse prevention hotline as adjunct to self-help manuals for long-term smoking cessation among self-quitters; (2) evaluate relative effectiveness of various smoking relapse prevention hotline interventions for self-quitters; and (3) assess determinants of relapse vs. abstinence in self-quitters.
Methods or Approach:
The relative effectiveness of three relapse prevention interventions offered by a community-based hotline service that targets self-quitters is being examined. The most effective will be used in study 2, in which 10 counties will be randomly assigned to either self-help manual or self-help manual and access to the hotline. Subjects will be followed for up to 3 years. Both studies will assess factors related to relapse or maintained abstinence. Hotline callers will be interviewed at or near the time of a relapse episode, and recontacted at various followup intervals.
Results to Date:
Preliminary results suggest that negative affect is a frequent precipitant to relapse; persons who call when tempted to smoke are more likely to be abstinent at 1- and 3-month followup than callers who have already smoked. Counselor's confidence ratings of caller's ability to remain abstinent differentiate smokers from abstainers at 1-week followup.
Project Dates:
August 1984–July 1988.
Financial Support:
NCI (1R01CA38238-01); ALA.

1290. USA MEDDAC WUERZBURG, Department of Ambulatory Patient Care - Nursing, APO New York, New York 09801.

Project Title:
The Effect of Cigarette Smoking on Army Physical Readiness Test Performance of Enlisted Army Medical Department Personnel.

Principal Investigator:
Jensen, R.G.
Objective:
To determine the effect (if any) of cigarette smoking on the service member's physical readiness test performance.
Methods or Approach:
It is assumed that test performance reflects physical fitness and that physically fit soldiers are more effective soldiers. In March 1984, 100 smoking-related questionnaires were randomly distributed at a Medical Company formation; 66 were returned. In April, the hospital conducted a three-event physical performance test consisting of pushups, situps, and a 2-mile run. Following posting of PT test scores, the questionnaires were used to divide subjects into present smokers, ex-smokers, and nonsmokers. Scores among the various groups were compared to test for variance.
Results to Date:
In both male and female subgroups, nonsmokers scored higher than smokers in all three events, although statistical significance was not determined. Results have been submitted for publication.

Project Dates:
March 1984–April 1984.
Financial Support:
USA MEDDAC Wuerzburg.

1291. USDA, ARS, CORNELL UNIVERSITY, Ithaca, New York 14853.

Project Title:
Analytical Procedures for the Estimation of Nonvolatile N-Nitrosamines and Their Precursors in Foods.

Principal Investigator:
Hotchkiss, J.H.
Objective:
To (1) develop an improved, simple, rapid method to estimate nitrite (NO_2) and nitrate (NO_3) content of complex food samples with a minimum of sample preparation; (2) develop a multidetection procedure for neutral and ionic lower molecular weight nonvolatile N-nitroso compounds in foods; and (3) investigate the possible formation of these compounds during food processing and preparation.
Methods or Approach:
A procedure will be developed that will efficiently extract NO_2 and NO_3 from a variety of foods. Benzene will be nitrated to form nitrobenzene, which is then detected by gas chromatography (GC). Nitrite will be oxidized to NO_3 and analyzed by difference. A TLC procedure for screening N-nitrosoamino acids in foods and a confirming procedure based on methylation of the acids with detection by GC-thermal energy detection (TEA) will be developed. Nonvolatile high and low molecular weight N-nitroso compounds will be investigated in fried-out bacon fat.
Results to Date:
New analytical techniques are currently being developed to estimate occurrence of NO_3 in foods and other biological materials. NO_3 is the major source of nitrosating agent in the diet and is most likely responsible for in vivo formation of N-nitrosamines, which has been shown to occur in humans. These techniques are based on the aqueous nitration of benzene to form nitrobenzene, which is subsequently detected by GC and either flame ionization (FID) or TEA. FID detection is widely available and simple; TEA detection is at least 10 times more sensitive and highly specific. Tracer studies utilizing benzene nitration and N-labeled NO_3 with subsequent analysis by GC-MS have been used to study biological disposition of NO_3. NO_3 biosynthesis has been demonstrated in the ferret. An extraction and cleanup procedure with subsequent nitrobenzene formation was developed to assay several dried foods for NO_3. The sensitivity of the assay is from 100 to 200 μg/kg. Coefficients of variation ranged from <2 percent to 12 percent at NO_3 levels of 5 to 50 mg/kg. Dried milks, whey, cocoa, infant formula, coffee creamers, buttermilk, and tobacco snuff were included in the survey. Concentrations ranged from 0.7 (dry milk) to 13,000 mg/kg (snuff). A simple column extraction procedure for extracting N-nitrosoamino acids from aqueous samples has been developed.
Project Dates:
June 1983–September 1986.
Financial Support:
USDA (NYC-143412).
References:
(1) Ross, H.D.; Hotchkiss, J.H. "Analysis of Nitrate and Nitrite in Dried Foods by GC-Thermal Energy Analyzer." 97th Meeting of the Association of Official Analytic Chemists, Washington, D.C., 1983, p. 40. (Abstract). (2) Dull, B.J.; Hotchkiss, J.H. "A Rapid Gas Chromatographic Method for the Estimation of Nitrate in Biological Samples Using Flame Ionization and Thermal Energy Analyzer Detectors." *Food Chemistry and Toxicology* (In press). (3) Havery, D.C.; Hotchkiss, J.H.; Fazio, T. "A Rapid Method for the Determination of Volatile N-nitrosamines in Liquid and Dried Foods." *International Agency for Research in Cancer* (45):219, 1983. (4) Webb, K.S.; Libbey, L.M.; Hotchkiss, J.H., et al. "Mass Spectrometric Analysis of N-Nitroso Compounds and Derivatives." *International Agency for Research in Cancer* (45):449, 1983.

1292. USDA, ARS, PLUM ISLAND ANIMAL DISEASE CENTER, Orient Point, New York 11944.

Project Title:
Plant Growth Regulators to Control Tobacco Growth and Development.

Principal Investigators:
Steffens, G.L.; Meudt, W.J.; Buta, J.G.
Objective:
To discover, evaluate, and determine effects of natural and synthetic plant growth regulators for utilization on tobacco to increase production efficiency.
Methods or Approach:
Effects of applied natural and synthetic chemicals, including combinations of chemicals, will be evaluated on tobacco axillary and terminal bud growth and on other plant growth and development characteristics. The most promising components from natural materials will be isolated and characterized. Analogues of active compounds will be synthesized to study structure-activity correlations. Interactions of isolated natural products with known plant growth hormones will be studied to provide a broader understanding of the growth of the tobacco plant and its control.
Results to Date:
Studies were made of combinations of growth regulators to lower the amount of maleic hydrazide (MH) necessary to control sucker growth on tobacco for reduction of chemical residue levels because of smoking and health consideration. Gibberellic acid applied prior to MH tended to reduce the amount of MH required to control tobacco sucker growth. Endolhall, chlormequat, abscisic acid, chlorothalonil, "AMO-1618," chlorofluorenol, "Bualta," NAA, beta NAA, and daminozide combined with low levels of MH did not effectively control sucker growth on field-grown tobacco. However, CGA-41065 N-ethyl-N-(2-chloro-6-fluoro-benzyl)-2',6'-dinitro-4'-trifluoromethylaniline applied to tobacco in ad hoc Regional Tobacco Growth Regulator field experiments was effective at 12 locations and is considered effective enough to be further developed into a commercial product with the hopes that residue levels and health problems will be minimal. Several dinitroanaline-related compounds were also found to be effective tobacco sucker control agents in cooperative studies; extracts of plants have been utilized to find new biologically active chemicals for the regulation of plant growth. Of over 300 species evaluated, about 10 percent controlled tobacco sucker growth by 80 percent or more (weight basic). Camptothecin and harringtonolide, which were isolated in sufficient quantities for small scale field trials, resulted in tobacco sucker growth inhibition.
Project Dates:
January 1974–April 1982.
Financial Support:
USDA (1109-20072-001).

1293. VETERANS ADMINISTRATION MEDICAL CENTER, MOUNT SINAI SCHOOL OF MEDICINE, 130 West Kingsbridge Road, Bronx, New York 10468.

Project Title:
Pathologic and Toxic Effects of Alcohol. Alcohol and Carcinogenesis.

Principal Investigators:
Wolf, J.; Lieber, C.S.; Garro, A.
Objective:
To determine whether chronic administration of ethanol to rats might increase pulmonary activation of procarcinogens in tobacco pyrolysates and smoke condensates that, when activated by microsomes, have been shown to be mutagenic.
Methods or Approach:
Adult male Sprague-Dawley rats were pair-fed nutritionally adequate liquid diets (containing 36 percent of total calories either as ethanol or isocaloric carbohydrates) for 3 to 4 weeks. Rats were sacrificed after an overnight fast; lungs were removed and microsomes were prepared. Tobacco pyrolysate was prepared from commercially available cigarette tobacco that was heated under vacuum at 500° for 1 min. Microsomal activation of procarcinogens/promutagens to mutagenic derivatives was assayed with *Salmonella typhimurium* His^- strain TA 100 (Ames et al.). In this assay, activation of promutagens results in an increase in the number of His^+ revertants that are counted as colonies growing on a histidine deficient medium.
Results to Date:
No difference was detected in benzo(*a*)pyrene (BaP) monooxygenase activity between alcohol-fed and control animals; lung microsomes from both groups of animals activated BaP to the same degree. However, when lung microsomes from ethanol-fed rats were incubated with tobacco pyrolysate, an enhanced activation to mutagenic derivatives was observed. Since no difference was seen in BaP activation, compounds in tobacco pyrolysate other than BaP must be incriminated for the difference in mutagenicity. The active compounds have not been identified, but may include pyrolysis products of peptides or some amino acids or nitrosamines that have been detected in trace amounts in tobacco.
Project Dates:
December 1977–November 1982.
Financial Support:
NIAAA (AA 03508).

1294. VETERANS ADMINISTRATION MEDICAL CENTER, 3495 Bailey Avenue, Buffalo, New York 14215.

Project Title:
Health Promotion of Patients With Peripheral Vascular Disease.

Principal Investigators:
Ventura, M.R.; Young, D.; Feldman, M.J., et al.
Objective:
To determine whether patients in an intervention program would improve exercise and foot care habits, reduce smoking, and have fewer peripheral vascular disease-related illnesses than patients not receiving the intervention.
Methods or Approach:
Patients with ankle/brachial pressure indices of < 1.0 on one or both legs were randomly assigned to the experimental ($n=42$) or control ($n=44$) group. All 86 patients were assessed on a variety of health-related and activity behaviors prior to and 26 weeks after enrollment. Experimental group patients worked with professionals on selecting programs designed to modify and improve smoking, exercise, and foot care habits.
Results to Date:
At the end of 26 weeks, chi-square analysis showed no significant differences between experimental and control groups or changes in smoking and foot care, although results were in the anticipated direction. Of those who made some change in smoking habits, 10 were in the experimental group and 4 were controls. Study patients who increased exercise showed greater increases than control patients in frequency ($p=0.001$), distance ($p=0.007$), and length ($p=0.002$) of walks.
Project Dates:
January 1982–March 1983.
Financial Support:
VA (444-2).

1295. VETERANS ADMINISTRATION MEDICAL CENTER, 3495 Bailey Avenue, Buffalo, New York 14215.

Project Title:
Epidemiologic Study of Lung Cancer in Non-Smokers.

Principal Investigators:
Janerich, D.T.; Montes, M.
Objective:
To determine what fraction, if any, of lung cancers among nonsmokers can be explained by passive smoking and occupation; determine whether other risk factors could be identified that are responsible for a significant proportion of lung cancer cases among nonsmokers.
Methods or Approach:
It has been suggested that the rate of lung cancer may be increasing among nonsmokers and that passive inhalation of a spouse's cigarette smoke may double a nonsmoker's risk of getting lung cancer. In addition, there is some evidence that the risk of lung cancer in certain occupations is higher among nonsmokers than among smokers. A population-based case-control epidemiologic study will compare 450 lung cancer patients who have never smoked with 450 matched nonsmoking controls. Personal interviews will be used to collect data on passive smoking, history of occupational exposures, environmental exposures, dietary Vitamin A and B-carotene, history of obstructive lung disease, and family history of lung cancer. Using a pathologic and clinical review of 450 nonsmoking lung cancer cases matched to an additional 450 smoking lung cancer cases, duration and type of symptoms, operability, survival, location of tumors, and histologic type will be compared. The proposed study has potential applications not only in prevention, diagnosis, and treatment of lung cancer among nonsmokers, but also in discovering risk factors for lung cancer in general. It may be able to detect factors that are overshadowed in other studies by the strong influence of smoking.
Results to Date:
Project is in a preliminary phase.
Financial Support:
VA.

1296. VETERANS ADMINISTRATION MEDICAL CENTER, 800 Poly Place, New York 11219.

Project Title:
Biochemical Markers in Emphysema.

Principal Investigator:
Dulfano, M.J.

Objective:
To identify biochemical indicators that can help assess the cause and/or progression of alveolar destruction in patients with emphysema.
Methods or Approach:
The concentrations of gamma glutamyltranspeptidase, elastase, amylase, and albumin in pulmonary lavage secretions will be studied. Findings will be related to type and severity of chronic obstructive pulmonary disease.
Results to Date:
Project has been started and 50 patients have been processed.
Future Plans:
Analysis of the material will be done after more patients have been enrolled.
Financial Support:
VA.

1297. VETERANS ADMINISTRATION MEDICAL CENTER, 4081 First Avenue, New York, New York 10010. BELLEVUE-NYU MEDICAL CENTER, First Avenue at 27th Street, New York, New York 10016.

Project Title:
Coordinated Activities of Ceruloplasmin, Ferrous Ion Transferrin in Defense of the Lung Against Free Radicals.

Principal Investigators:
Aranda, C.P.; Galdston, M.
Objective:
To (1) define the causal relationship between derangement in function of the extracellular antioxidant defense and that of the antielastase defense in the lower respiratory tract and in the circulation; (2) investigate the defenses in healthy nonsmokers and in smokers and ex-smokers with and without chronic obstructive pulmonary disease (COPD); (3) learn whether defenses are related to pack-years smoked, are determinants of COPD, and regress on cessation of smoking; (4) delineate coordinated activities of the constituents of the antioxidant defense by investigating effect of transferrin concentration and available iron-binding capacity plus trace amounts of ferrous ion on the capacity of ceruloplasmin to prevent suppression of the elastase inhibitory capacity of α_1-protease inhibitor (α_1PI) by whole cigarette smoke and degradation of representative biologically relevant substrates and to restore the elastase inhibitory capacity of oxidized α_1PI; and (4) investigate mechanisms of inactivation of antioxidant activity of ceruloplasmin by whole cigarette smoke, cigarette smoke solution, and cigarette tar.
Methods or Approach:
Volunteers will be distributed in five groups, 40 in each group, as follows: healthy individuals who never smoked, smokers with COPD, smokers without COPD, ex-smokers with COPD, and ex-smokers without COPD. All volunteers will undergo venipuncture for withdrawal of 15 ml blood, spirometric pulmonary function tests of forced vital capacity, and flow-volume loops. It is estimated that 50 to 70 patients from the VA will be recruited for this study. Matched pairs of serum and bronchoalveolar lavage concentrate will be analyzed for (1) major protein content; (2) concentration of ceruloplasmin, transferrin, and α_1PI; (3) iron-binding capacity and unsaturated iron-binding capacity; (4) antioxidant activity; and (5) α_1PI elastase inhibitory capacity.
Results to Date:
Project is in a preliminary phase.
Financial Support:
VA.

1298. VETERANS ADMINISTRATION MEDICAL CENTER, Middleville Road, Northport, New York 11768.

Project Title:
In Vivo Measurement of Cadmium and Other Metals by Prompt-Gamma Neutron Activation Analysis.

Principal Investigator:
Cohn, S.H.
Objective:
To measure cadmium (Cd) levels in vivo; compare Cd levels in smokers and nonsmokers.
Methods or Approach:
Absolute levels of Cd in the kidney and concentration of Cd in the liver were measured in vivo in 20 healthy adult males. Cd content of livers and kidneys was measured by prompt-gamma neutron activation analysis, using ^{238}Pu,Be neutron sources.
Results to Date:
Organ Cd levels of smokers were significantly elevated above those of nonsmokers. Average total body burden of Cd in men at age 50 was estimated to be 19.3 mg for nonsmokers and 35.5 mg for smokers (38.7 pack-year smoking index). Biological halflife for Cd in the body was estimated to be 15.7 (range, 10 to 33) years. Cigarette smoking was estimated to result in absorption of 1.9 µg Cd/pack. No relationship was found between body stores of Cd (liver and kidney) and Cd or β-microglobulin levels in urine and blood.
Future Plans:
Currently, the neutron activation facility is being mounted on a 34-foot mobile trailer unit. With the support of ILZRO, this unit will be used to monitor levels of Cd in industrial workers. The relative expense and sophisticated expertise required to mount such a program may limit availability of the technique to small-scale research-oriented needs. Nevertheless, it is anticipated that critically important data, particularly on industrially exposed workers, will provide a better basis for determining critical concentrations and for revising standards for industrial and environmental Cd pollution.
Financial Support:
VA.

1299. VETERANS ADMINISTRATION, 408 First Avenue, New York, New York 10010.

Project Title:
American Health Foundation Epidemiological Studies.

Principal Investigators:
Spritz, H.; Wynder, E.L.
Objective:
To identify and examine the effect of risk factors associated with cigarette smoking, plus confounding factors, on lung, bladder, and pancreatic cancer, myocardial infarction, and cancers of the upper respiratory and upper alimentary tracts; determine risk of various tobacco-related diseases for individuals with long histories of smoking filtered cigarettes in general and low tar/low nicotine-yielding cigarettes in particular.
Methods or Approach:
The effects of smoking cigarettes with varying levels of tar and nicotine on the risk of disease will be measured and the use of the newer "less hazardous" cigarettes will be monitored. Questionnaires are administered to hospitalized patients with an index case disease, and to hospitalized controls, in 18 U.S. hospitals. The major parameters of tobacco usage investigated include (1) type, duration, and amount of tobacco used by brand; (2) tar and nicotine yields of cigarettes smoked; (3) inhalation practices; and (4) length of cigarette smoked.

Results to Date:
Data are being analyzed in relation to various demographic characteristics, and risk ratios are being calculated. A total of 1,250 cases and an equal number of hospital controls are interviewed annually.
Financial Support:
VA.

1300. VETERANS ADMINISTRATION, Beacon Street, Castle Point, New York 12511.

Project Title:
A Study to Evaluate the Effectiveness of a Smoking Cessation Program.

Principal Investigator:
Teders, S.J.
Objective:
To (1) evaluate the effectiveness of a smoking cessation treatment program; (2) develop a programmatic followup procedure that will analyze the causes of smoking relapse and treat its occurrence; and (3) evaluate the effects of smoking cessation on vascular and pulmonary parameters.
Methods or Approach:
Patients whose medical conditions are caused or made worse by smoking are referred to the project by their attending physicians. A 2-week assessment to detail the cognitive, physiological (addictive), behavioral, and situational factors that operate to maintain smoking in the individual case is conducted. An 8-week therapy period is then conducted to apply therapeutic strategies that are designed to modify the specific factors that maintain smoking in the individual. Finally, subjects are followed up by telephone on a monthly basis for 1 year to document incidences of relapse and to treat their occurrence. Blood plasma cotinine levels will be collected and analyzed at pretreatment and again at 6 months posttreatment in order to measure smoking rate and change in smoking behavior. The Coping Responses to Smoking Questionnaire, Problem Assessment Questionnaire, Smoking Patterns Questionnaire, Rating of Treatment Rationale, Why Do You Smoke Questionnaire, State-Trait Anxiety Questionnaire, Beck Depression Inventory, and the Buss-Durkee Hostility Inventory will be utilized at pretreatment to aid in elucidating the variables maintaining cigarette smoking in each individual. Various pretreatment and posttreatment measures of pulmonary and vascular functioning will also be performed.
Results to Date:
Project is in a preliminary phase.
Project Dates:
May 1984–continuing.
Financial Support:
VA.

1301. VETERANS ADMINISTRATION, Middleville Road, Long Island, Northport, New York 11768.

Project Title:
Relationship Between Smoking During Group Therapy and Verbalization of Anger.

Principal Investigator:
Parker, B.D.
Objective:
To test the hypothesis that when people do not smoke in psychotherapy group sessions there will be a significant increase in their verbalization of angry feelings.
Methods or Approach:
Patients from three psychotherapy groups on different inpatient psychiatric units will serve as subjects. Groups are composed of patients who have been recommended for group therapy by the interdisciplinary treatment team of the respective unit. A survey of all the study participants will be conducted to determine smoking patterns prior to data collection. In the three experimental groups smoking will be prohibited for six group therapy sessions and then allowed for six group therapy sessions during the scheduled group psychotherapy hour conducted by the nurse therapists on the Psychiatric Inpatient Units. The Moos Group Environment Scale will be completed by each patient in the three groups before the study begins and after the sixth and twelfth group therapy sessions. The statistical measure to be applied is the two-factor mixed design: repeated measures on one factor. The groups will be tape-recorded so that the feelings of anger that are verbalized in the therapy hour may be tallied by an independent rater. This tally has been checked for inter-rater agreement by four different raters and has a inter-rate agreement rate of 90 percent. The principal investigator and an independent rater will record the incidence of smoking during the therapy sessions. The incidence of smoking and the verbalizations of feelings of anger will be correlated with the findings from the survey regarding smoking and the Group Environment Scale.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1984–continuing.
Financial Support:
VA.

1302. VETERANS ADMINISTRATION, Old Albany Post Road, Montrose, New York 10548.

Project Title:
The Effect of Alcohol Withdrawal on Smoking Behavior in an Alcohol-Dependent Population.

Principal Investigators:
Stetson, D.E.; Schneider, S.J.
Objective:
To (1) examine, in an inpatient alcohol-dependent population, the effects of abstinence from alcohol on cigarette smoking rate and on cigarette smoking topography; (2) examine changes in the circulating level of the neurohormone prolactin during alcohol withdrawal; and (3) correlate such changes with observed cigarette smoking patterns.
Methods or Approach:
Four indices of smoking topography will be measured: number of puffs per cigarette, puff duration, interpuff interval, and puff volume. Three response systems will be monitored by well-established techniques: motoric (nicotine intake), self-report (anxiety), and physiological (serum prolactin concentration). The experimental group will consist of male smokers, ages 21 to 60, admitted to the Franklin Delano Roosevelt Veterans Hospital with a principal diagnosis of alcohol dependence. These subjects will be inpatients on a 30-day alcohol rehabilitation unit. Male nonalcohol-dependent smokers will be recruited from new hospital admissions to serve as an inpatient hospitalization control group. Smoking, anxiety, and prolactin will be measured upon hospital admission and will be repeated on weekly basis for 4 consecutive weeks.
Results to Date:
Difficulties in recruiting nonalcohol-dependent subjects free of medications affecting the prolactin and anxiety variables precluded the inclusion of the hospital control group in the study. Twenty alcohol-dependent subjects have been studied.

Preliminary analyses indicate that during the abstinence period no significant changes in intrasubject smoking rate nor calculated nicotine intake occurred. Also, no statistically significant relationships were found among the anxiety, prolactin, and nicotine intake measures during the withdrawal and post-withdrawal periods. Further data analysis is in progress.

Financial Support:

VA.

1303. YESHIVA UNIVERSITY, ALBERT EINSTEIN COLLEGE OF MEDICINE, 1300 Morris Park Avenue, Bronx, New York 10461.

Project Title:

Preparation and Method of Use of Enzyme Effective for Conversion and Detection of Carbon Monoxide.

Principal Investigator:

Scheinberg, I.H.

Objective:

To perfect a method for using the enzyme carbon monoxidase (CMase) for detection and conversion of carbon monoxide in a gas stream, the gas stream of particular interest being tobacco smoke.

Methods or Approach:

CMase is derived from blood, bacteria, and plants, in which the enzyme is widely distributed. The enzyme can be utilized as a component of the whole organism or can be isolated from the bacterium or plant following rupture of the cell wall. The resulting suspension can be centrifuged into soluble and insoluble fractions and location of CMase determined. The fraction containing the soluble enzyme is subjected to standard protein fractionation procedures. The protein can then be absorbed on a support such as charcoal, cellulose, or Sepharose and similar gels to form a filter.

Results to Date:

CMase is effective for conversion of CO in a gas stream. Where conversion is the step of oxidizing CO to CO_2, CMase can be used to detect CO. Production of CMase can be accelerated by growing bacterial cultures or plants in an atmosphere containing an increased concentration of CO. Increasing oxygen concentration simultaneously is also beneficial. A filter medium including CMase can substantially decrease CO concentration in the gas phase of tobacco smoke. Combining CMase in a filter with compounds that reversibly bind CO presents additional advantages.

Reference:

Scheinberg, I.H. *Preparation and Method of Use of Enzyme Effective for Conversion and Detection of Carbon Monoxide.* U.S. Patent No. 4,071,037, January 31, 1977, 8 pp.

North Carolina

1304. USDA, AGRICULTURAL RESEARCH SERVICE, TOBACCO RESEARCH LABORATORY, Oxford, North Carolina 27565.

Project Title:

Biological Research to Reduce Hazards From Chemical Pesticides and Tobacco Smoke.

Principal Investigator:

Spurr, H.W., Jr.

Objective:

To develop biological procedures to reduce dependency on chemical pesticides for plant disease control; study effects of microorganisms on chemical composition and health hazards of tobacco smoke.

Methods or Approach:

Relationships among nonpathogenic microorganisms, bacteria, and fungi and normal plant growth and disease development will be determined and this knowledge will be used to manipulate and manage plant microflora. The effect of microorganisms in tobacco leaves on constituents of smoke and the ensuing impact on smokers will be assessed, giving primary emphasis to developing information on mutagenicity of smoke using the Ames biological assay and applying this information to reduce or eliminate mutagenic activity in smoke.

Results to Date:

The 1979 and 1980 blue mold epidemics were characterized by extensive disease in the field and a high incidence of systemic infection. Tissues from diseased North Carolina burley and flue-cured tobacco were examined microscopically for pathogen structures, especially oospores. Oospores were atypical; they were spherical with a mean diameter of 24 µM, readily stainable, hyaline, and had a medium-thick cell wall. The wall was echinulate, covered with blunt-tipped bumps uniformly distributed over the surface. Widespread field infection, extensive systemic infection, and different oospore morphology indicate a new race of the pathogen causing the epidemics. A selective medium was used to identify and count *Pseudomonas cepacia* in mixed populations from soil extracts or plants. Soil and mature tobacco roots were sampled in coastal plain, piedmont and mountain areas of North Carolina. *P. cepacia* was 10^3 to 10^5 colonies or 0.4-2.6 percent of the extracted bacterial population. Total bacteria counts on tobacco roots were 10^5 to 10^7 colony-forming units (CFU)/cm^2 root surface area; *P. cepacia* was 10^2 to 10^4 CFU or 0.1 to 1.0 percent of the population. Mutagenic activity, condensate level, and nicotine level were determined in cigarette smoke from 13 selected tobaccos. Mutagenic activity ranged from 2,500 to 9,200 mutants/g, condensate from 16 to 32 mg/g, and nicotine from 0.5 to 8 mg/g tobacco smoked. There was no association between mutagenic activity and either condensate level or nicotine level.

Project Dates:

October 1979–June 1984.

Financial Support:

USDA (6647-20881-012D).

References:

(1) Chaplin, J.F.; Spurr, H.W., Jr. "Altering Condensate Levels in Tobacco Smoke by Genetic Techniques." *Beitraege zur Tabakforschung International* 11:151-160, 1982. (2) Nesmith, W.C.; Cohen, Y.; Kuc, J., et al. "Field Evaluation of Systemic Resistance to Blue Mold in Tobacco Induced by Inoculations With the Blue Mold Pathogen." *Phytopathology* 72:360, 1982. (3) Spurr, H.W., Jr.; Gwynn, G.R., Chaplin, J.F. "Non-Correlation of Mutagenic Activity With Condensate or Nicotine Levels in Cigarette Smoke From Flue-Cured Tobaccos." In: Proceedings of the 36th Annual Tobacco Chemists' Research Conference, 1982, p. 12.

1305. DUKE UNIVERSITY MEDICAL CENTER, Box 3926, Durham, North Carolina 27710.

Project Title:
Psychosocial Factors and Outcome in Coronary Disease.

Principal Investigator:
Williams, R.B.
Objective:
To determine effects of certain psychological, social, and behavioral factors on selected outcomes in coronary heart disease (CHD).
Methods or Approach:
All patients undergoing diagnostic coronary angiography are assessed as to clinical, historical, and psychosocial characteristics. Smoking history is included as a part of the patient's history. Psychosocial assessment includes the Minnesota Multiphasic Personality Inventory (MMPI), social interaction and support scales, functional status indicators, Type A (coronary-prone) behavior pattern assessments, life stress change units, and state measurements of anxiety and depression. All data, including angiographic findings, are collected independently and stored on-line for interactive analyses. Patients are followed on an annual basis to determine pain status, major cardiovascular events, and/or death. Selected patients, returning to the followup clinic for evaluation, complete the above battery of psychosocial assessments with the exception of the MMPI. Hypotheses generated in this setting are extrapolated to other more representative, free-living populations.
Results to Date:
A major finding has been the relationship between coronary atherosclerosis and hostility as measured by the MMPI. In two subsequent replications of this finding, smoking was not found to be related to hostility, but both factors were found to be independently predictive of cardiovascular and overall mortality. Recent analyses of the data indicate a significant interaction between age and Type A (coronary prone) behavior pattern, while significant interactions are also found between age and smoking and sex and smoking. Overall, smoking was found to be more predictive at younger ages. Smoking increases risk for women more than it does for men, but overall risk for men is higher than for women. Findings are felt to underscore the need for validation in other more respresentative, free-living populations.
Future Plans:
Cononical discriminant function analyses are underway to determine those sets of behavioral variables, including smoking, which are independently related to CHD etiology and outcomes in an attempt to establish appropriate primary and secondary intervention strategies.
Project Dates:
May 1976–continuing.
Financial Support:
NHLBI (5R0118589-06).
References:
(1) Williams, R. B.; Haney, T. L.; Lee, K. L.; Kong, Y.; Blumenthal, J. A.; Whalen, R. E. "Type A Behavior, Hostility and Coronary Atherosclerosis." *Psychosomatic Medicine* 42: 539-549, 1980. (2) Barefoot, J. C.; Dahlstrom, W. G.; Williams, R. B. "Hostility, CHD Incidence and Total Mortality: A 25-Year Follow-up Study of 255 Physicians." *Psychosomatic Medicine* 45:59-63, 1983. (3) Shekelle, R. B.; Gale, M. "Hostility, Coronary Heart Disease and Mortality." *Psychosomatic Medicine* 45:109-114, 1983. (4) Williams, R.B.; Barefoot, J.C.; Haney, T.L., et al. "Age, Type A Behavior and CAD in an Angiographic Population." (Manuscript in preparation).

1306. DUKE UNIVERSITY MEDICAL CENTER, Box 3958, Durham, North Carolina 27710.

Project Title:
The Epidemiology of Childhood Rhabdomyosarcoma.

Principal Investigator:
Grufferman, S.
Objective:
To conduct a collaborative case–control study of childhood rhabdomyosarcoma (RMS); investigate potentially etiologic environmental factors.
Methods or Approach:
The following hypotheses will be evaluated: (1) the father's but not mother's cigarette smoking is a strong risk factor for RMS; (2) there is an inverse relationship between immunization status and RMS and a positive association between RMS and preventable infectious diseases; (3) environmental exposures to chemicals, mother's age at subject's birth, and family history of asthma are risk factors for RMS; and (4) there is an inverse association between RMS and socioeconomic status. The hypotheses, prompted by findings of a recent study of childhood RMS, will be refined and reevaluated, and the role of other environmental agents will be assessed. The role of heredity will also be investigated. New methods will be developed for the utilization of subjects from collaborative cancer clinical trials for etiologic research, which would greatly facilitate studies of both rare and common tumors by permitting rapid accrual of sufficient numbers of subjects and fostering greater interaction between epidemiologists and clinicians. The Intergroup Rhabdomyosarcoma Study will serve as a means of identifying cases. Between 350 and 400 new cases, aged 0 to 20 years, will be accrued over a 2-year intake period, representing approximately 65 percent of all new cases in the United States. All diagnoses will be subjected to central pathology review. Controls will be selected from the same communities as cases and will be of the same race and sex and of similar age. One control for each case will be identified by random digit dialing. All subjects will be interviewed by telephone. It is believed that the issue of environmental factors in the etiology of childhood cancers has not been adequately explored. The relatively short induction periods between potential etiologic exposures and disease manifestation in children provide unique opportunities for the study of environmental etiologic agents.
Results to Date:
Results are not yet available.
Financial Support:
NCI (5R01CA21244-04).

1307. DUKE UNIVERSITY MEDICAL CENTER, 4019 Roxboro Road, Durham, North Carolina 27704.

Project Title:
Cancer Communication Network: The Cancer Information Service.

Principal Investigator:
McGrath, D.
Objective:
To respond to callers who want to quit smoking to (1) offer encouragement; (2) assist caller to develop a plan; (3) use the Cancer Information Service (CIS) as a resource for information and assistance; and (4) refer callers to services/agencies that offer smoking cessation sessions/clinics.
Methods or Approach:
Callers are asked about smoking behavior (how much, how long, attempts to quit, what happened). The intention to quit is

reinforced, any success is commended, encouragement is offered, and callers are helped to develop a plan for quitting, offered printed information, referred to clinics when desired, and offered tips for success.

Results to Date:
Callers appreciate the time, information, and encouragement offered and are surprised and encouraged when told that several attempts to quit are a positive sign. The idea of developing a plan and how to do it and aspects of smoking behavior and ways to change are very favorably received.

Future Plans:
Ways to talk to callers and suggestions, particularly when smoking is used as a coping mechanism for stressful situations, will be developed.

Project Dates:
December 1984–November 1989.

Financial Support:
NCI (N01CN25575).

1308. DUKE UNIVERSITY MEDICAL CENTER, Box 31217, Durham, North Carolina 27710.

Project Title:
MMPI Predictors of Smoking Initiation and Cessation in a Sample of Physicians.

Principal Investigator:
Barefoot, J.C.

Objective:
To identify personality variables associated with smoking status; determine characteristics that prospectively predict smoking cessation.

Methods or Approach:
Current smoking status of 236 physicians was established by mail survey. MMPI scores, which had been obtained from the same men approximately 25 years before, were used to study retrospective correlates of smoking initiation and to identify prospective predictors of smoking cessation. Nonsmokers, ex-smokers, and current smokers were compared on a number of psychological dimensions suggested by the literature.

Results to Date:
The L, Pd, and Schubert smoking scales successfully discriminated doctors who had never become smokers from those who had. Stepwise logistic regression identified the Schubert scale as the best correlate of initiation. The Ma scale was the only measure to predict successful cessation. Among those who had not stopped smoking, the L and Pd predicted number of years that they would smoke. The Schubert scale, manifest anxiety, and ego-resilience also correlated with years smoked in univariate analyses.

Future Plans:
Findings will be validated in other populations. Item analyses of scales will be used in an attempt to improve predictive power.

Project Dates:
January 1982–continuing.

Financial Support:
NIMH (MH 15131; MH 70428).

1309. DUKE UNIVERSITY MEDICAL CENTER, Department of Medicine and Chemistry, Durham, North Carolina 27710. UNIVERSITY OF CHICAGO, Chicago, Illinois

Project Title:
Role of Keto Fatty Acids in Bronchitis.

Principal Investigators:
Lynn, W.S.; Lynn, D.G.

Objective:
To ascertain if keto oleates, whether produced by cotton, tobacco, or humans, are involved in epithelial differentiation.

Methods or Approach:
Toxins are isolated and characterized from lung lavage and lung of exposed persons, either in life or at autopsy. Toxins are identified by their effects on cultured mammalian cells. The identified organic and particulate toxins are then assessed by their effects on the cytotoxic and migratory activation of human inflammatory cells, i.e., blood neutrophils, monocytes, platelets, and alveolar macrophages. The same cytotoxins and inflammagens are being isolated from cotton bracts, cigarette smoke, and tobacco leaves.

Results to Date:
Four cytotoxic keto oleic acids have been identified in postmortem specimens from cotton workers; two are also present in cigarettes. All are powerful inflammagens and also activate myelocyte differentiation in vitro.

Future Plans:
Animals will be tested with keto oleates to determine whether chronic bronchitis develops. Tests will be done to ascertain whether keto oleates are incorporated into cellular membranes.

Project Dates:
June 1979–1988.

Financial Support:
North Carolina Lung Association; Cotton Incorporated.

1310. DUKE UNIVERSITY, MEDICAL CENTER, Box 2953, Durham, North Carolina 27710.

Project Title:
Epidemiology of Multiple Myeloma.

Principal Investigator:
Grufferman, S.

Objective:
To investigate the epidemiology of multiple myeloma (MM).

Methods or Approach:
The study has two major components, a medical record review of 350 MM cases and an interview study of an additional 150 MM patients, both components involving matched hospital controls. In addition to examining for associations with available demographic variables, associations between MM and socioeconomic class (S-E), occupation, environmental exposures, diet, and diseases causing immune stimulation will be evaluated. Particular attention will be paid to evaluation of the association between S-E class and MM. Data on tobacco use in cases and controls are also being collected.

Results to Date:
Project is in the analysis phase.

Project Dates:
May 1977–1983.

Financial Support:
NCI (2R01CA22104-04).

1311. EAST CAROLINA UNIVERSITY, SCHOOL OF MEDICINE, Department of Surgery, Greenville, North Carolina 27834.

Project Title:
Effect of the Alteration of Trace Elements in Tobacco on the Chemical Composition of the Resulting Smoke

Principal Investigators:
Maier, R.H.; Pories, W.J.

Objective:
To alter the trace element content of tobacco leaves by foliar sprays during growing or during processing of harvested, cured tobacco; determine transference pattern of altered trace elements from tobacco to resulting smoke.

Methods or Approach:
Two varieties of cigarette tobacco were sprayed in the field with various concentrations of different trace elements, singularly and in combination. The tobacco was harvested, flue-cured, and stored for chemical analysis and production of experimental cigarettes. Experimental cigarettes were smoked in a smoking machine and the gaseous phase retained for trace element analysis.

Results to Date:
Preliminary results indicate increased content of certain trace elements in the smoke, resulting from trace element alteration in the field.

Project Dates:
June 1984–continuing.

Financial Support:
East Carolina University School of Medicine.

1312. MOSES H. CONE MEMORIAL HOSPITAL, 1200 North Elm Street, Greensboro, North Carolina 27284.

Project Title:
Effect of Maternal Smoking on Neonatal Growth and Behavior.

Principal Investigators:
Gal, P.; Boer, H.R.; Carver, T., et al.

Objective:
To (1) evaluate the influence of maternal smoking on growth at birth of term infants; (2) examine effects of maternal smoking on feeding patterns of infants, behavior of neonates, and length of hospital stay; and (3) search for a possible nicotine withdrawal syndrome.

Methods or Approach:
Term newborns in a normal nursery were randomly selected and nurses were interviewed regarding feeding and behavior. Mothers were also interviewed regarding maternal drug use, maternal diseases, and infants' behavior and feeding. Smoking patterns were recorded and compared for feeding problems, irritability, and duration of hospital stay.

Results to Date:
Of the 61 mother–infant pairs studied, 34 mothers were nonsmokers, 19 smoked a pack of cigarettes/day or less, 5 smoked 1.5 packs/day, and 3 smoked 2 packs/day. Average hospital stay ranged from 4.0 days for nonsmokers to 6.0 for the heaviest smokers. There were no low birth weight infants born to nonsmokers; 21 percent of light and medium smokers had low birth weight infants; 40 percent of those smoking 1.5 packs/day had low birth weight infants. Irritability was also high among infants of heavier smokers. Vomiting occurred in two of the three infants born to women who smoked two packs of cigarettes/day. Infants of heavier smokers showed some withdrawal symptoms from other stimulants (e.g., amphetamine).

Project Dates:
September 1981–April 1983.

1313. NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, Epidemiology Branch, P.O. Box 12233, Research Triangle Park, North Carolina 27709.

Project Title:
Cancer Risk From Transplacental and Passive Exposure to Cigarette Smoke.

Principal Investigators:
Sandler, D.P.; Everson, R.B.; Wilcox, A.J.

Objective:
To (1) determine the feasibility of retrospectively obtaining childhood smoke exposure histories from adults with and without cancer; (2) determine if early life exposure to cigarette smoke increases overall cancer risk in adulthood; (3) investigate whether passive exposure to cigarette smoke in adulthood increases overall cancer risk; and (4) identify specific sites that may be more likely to be related to passive smoke exposure.

Methods or Approach:
Over 500 cancer cases, 500 cancer-free controls (friends or neighbors of cases), and 700 relatives of cases and controls (usually mothers) were interviewed by telephone to obtain lifetime smoke exposure histories. Individuals were asked if the mother smoked at any time (during pregnancy or the study subject's childhood). Participants were also asked about smoking habits of fathers, other household members during childhood, and spouses. Data from parallel interviews with relatives of study subjects were used to evaluate the quality of the smoke exposure histories provided by adult offspring.

Results to Date:
Retrospective study of cancer risk from early life exposure to cigarette smoke proved to be feasible; qualitative information provided by cases on smoking by parents was surprisingly accurate. Smoking by fathers was associated with a 50 percent increase in overall cancer risk in adulthood and smoking by spouse was associated with a 60 percent increase in overall cancer risk. Smoking by the mother was associated with only a very slight increase in overall risk, but was strongly related to risk of leukemia and lymphoma. Cancer risks associated with passive smoke exposure were increased for smokers and nonsmokers and were not limited to known smoking-related sites. Cancer risks were also found to increase with increasing exposure to cigarette smoke.

Future Plans:
The study has been completed, but methods evaluated will be applied in future studies of specific cancer sites.

Project Dates:
July 1981–July 1984.

Financial Support:
NIEHS.

References:
(1) Sandler, D.P.; Everson, R.B.; Wilcox, A.J. "Passive Smoking in Adulthood and Cancer Risk." *American Journal of Epidemiology* (In press). (2) Sandler, D.P.; Everson, R.B.; Wilcox, A.J., et al. "Cancer Risk in Adulthood From Early Life Exposure to Parent's Smoking." *American Journal of Public Health* (In press). (3) Sandler, D.P.; Wilcox, A.J.; Everson, R.B. "Cumulative Passive Exposure to Cigarette Smoke and Cancer Risk." *American Journal of Epidemiology* 120:482, 1984 (Abstract).

1314. NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, Epidemiology Branch, P.O. Box 12233, Research Triangle Park, North Carolina 27709. JOHNS HOPKINS UNIVERSITY, SCHOOL OF HYGIENE AND PUBLIC HEALTH, Baltimore, Maryland 21205.

Project Title:
Cancer Risk in Persons Living With Smokers.

Principal Investigators:
Sandler, D.P.; Comstock, G.W.; Helsing, K.J.
Objective:
To determine mortality patterns and cancer incidence in relation to household exposure to cigarette smoke.
Methods or Approach:
A cohort of 60,000 individuals for whom information about smoking habits of household members was obtained in 1963 will be followed through the use of existing records to determine death rates, specific causes of death, and cancer incidence through 1975. Death rates and cancer incidence rates for adults living with smokers will be compared with those for persons not living with smokers.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–continuing.
Financial Support:
NIEHS.

1315. NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, LABORATORY OF PHARMACOLOGY, P.O. Box 12233, Research Triangle Park, North Carolina 27709.

Project Title:
Benzo(*a*)pyrene Biotransformation in Individual Hepatocytes.

Principal Investigators:
Massey, T.E.; Devereax, T.R.; Fouts, J.R.
Objective:
To develop a method for determining rates of xenobiotic biotransformation in individual cells; determine heterogeneity in rates of biotransformation between and within cell populations in mixed-cell preparations.
Methods or Approach:
Benzo(*a*)pyrene (BaP) disappearance was monitored in freshly isolated rabbit hepatocytes by microspectrofluorometry, using 372 nm excitation and 407 nm emission.
Results to Date:
In hepatocytes from untreated rabbits, incubation with 3.0 μmol BaP followed by washing the cells resulted in apparent first-order elimination of substrate. This elimination could be inhibited by coincubation with an inhibitor of BaP metabolism such as ellipticine or α-naphthoflavone. The rate of BaP biotransformation was increased by treatment with β-naphthoflavone prior to isolation of hepatocytes.
Future Plans:
The method will be applied to freshly isolated pulmonary cells to evaluate relative contributions to BaP biotransformation of different cell types.
Project Dates:
July 1984–July 1986.
Financial Support:
NIEHS.

1316. NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, LABORATORY OF PHARMACOLOGY, P.O. Box 12233, Research Triangle Park, North Carolina 27709.

Project Title:
Biotransformation of Xenobiotics in Enriched Populations of Rabbit Tracheal Ciliated Cells.

Principal Investigators:
Massey, T.E.; Fouts, J.R.
Objective:
Develop a method for purification of rabbit tracheal ciliated cells; determine the capacity of this cell type to carry out biotransformation reactions.
Methods or Approach:
Following protease digestion of tracheal lumen tissue, isolated cells were subjected to centrifugal elutriation and two-polymer (dextran-polyethylene glycol) phase separation for enrichment of ciliated cell fraction. Mixed-function oxidase activity was determined on purified cells by measuring 7-ethoxycoumarin (7-Ec) deethylase and coumarin hydroxylase activities.
Results to Date:
A highly enriched ciliated cell fraction (84 percent ciliated cells) was prepared. Enzyme activities (152 pmol/min/mg protein for 7-Ec deethylase and 32 pmol/min/mg protein for coumarin hydroxylase) could not be attributed to the presence of contaminating Clara cells, indicating that ciliated cells do contain some mixed-function oxidase activity.
Project Dates:
March 1984–December 1985.
Financial Support:
NIEHS.

1317. NORTH CAROLINA AGRICULTURAL AND TECHNICAL STATE UNIVERSITY, TOBACCO AND PESTICIDE RESEARCH, Greensboro, North Carolina 27411.

Project Title:
Pesticide Residues in Tobacco and Tobacco Smoke.

Principal Investigator:
Chopra, N.M.
Objective:
To investigate (1) amount of pesticides in cured tobacco; (2) transfer rates of pesticides into tobacco smoke; (3) breakdown products of pesticides and amounts present in tobacco smoke; and (4) types of reactions that take place in cigarette smoke.
Methods or Approach:
Tobacco is grown in experimental plots and treated with different amounts of pesticides under investigation. Tobacco leaves are harvested and flue-cured, manufactured into cigarettes, and smoked. The amounts of pesticides in tobacco and cigarette smoke are estimated and transfer rates are determined. The presence of pesticide breakdown products in cigarette smoke is investigated and amounts are determined. Various compounds, including some that are present in tobacco, are pyrolyzed at 860±25° C and pyrolysates are examined for presence of various compounds. Reaction mechanisms involving pyrolysis of substrates are determined.
Results to Date:
Results have been published.
Financial Support:
USDA (NC-x-039580223-02).
References:
(1) Chopra, N.M.; Rao, A.V.; Verma, M.M. "Study on the Pyrogenesis of PAHs in Cigarette Smoke: Pyrolysis of 1,3-

Butadiene + Ethylene Mixture in a Nitrogen Atmosphere." In: *Proceedings of the 8th International Tobacco Scientific Congress*, Vienna, Austria, October 7-12, 1984. (2) Chopra, N.M.; Alkubaisi. "Study on the Pyrogenesis of PAHs in Cigarette Smoke." In: *Proceedings of the 8th International Tobacco Scientific Congress*, Vienna, Austria, October 7-12, 1984.

1318. NORTH CAROLINA STATE UNIVERSITY, P.O. Box 7625, Raleigh, North Carolina 27695.

Project Title:
Development of Instrumentation for Measuring Quality and Composition of Tobacco.

Principal Investigator:
McClure, W.F.

Objective:
To (1) investigate the physical properties of tobacco; (2) develop reliable instruments for measuring quality and/or composition; (3) develop new analytical procedures and instrumentation for enhancing the processing of tobacco; and (4) design and develop transducers, manipulators, and computer vision systems for grading tobacco and tobacco products.

Methods or Approach:
Emphasis has been to exploit near infrared (NIR) technology for measuring chemical composition, which has involved development of hardware and software for relating spectral information to chemical composition. Fourier analysis of spectral data is being explored.

Results to Date:
The need for a rapid means of measuring chemical composition of tobacco lead to development of COMP/SPEC, a computerized NIR spectrophotometric facility. The facility has demonstrated that chemistry of tobacco can be determined directly from information gleaned from an NIR reflectance spectrum of pulverized leaf. Standard errors of estimate found were nicotine, ±0.175 percent (range of concentration 1.6 to 4.4); nitrogen, ±0.125 percent (range 1.5 to 3.1); sugars, ±0.995 percent (range 4 to 24); water-soluble nitrogen, ±0.146 percent (range 0.63 to 1.62); calcium, ±0.176 percent (0.96 to 3.20); and potassium, ±0.15 percent (range 2.34 to 3.84 percent). Use of Fourier transforms has reduced computer time by 96 percent and has cut storage requirements by 98 percent.

Future Plans:
Efforts will continue to develop and refine NIR spectroscopy for measuring composition, and to develop software for tobacco type identification and to enhance the system for detection of toxic substances such as pesticides.

Project Dates:
October 1984–October 1989.

Financial Support:
Tobacco Foundation; Tobacco Research Funds: Tobacco Institute.

1319. NORTH CAROLINA STATE UNIVERSITY, Box 8110, Raleigh, North Carolina 27695.

Project Title:
Demand for Tobacco and Tobacco Products. Tobacco Supply Conditions and Industry Structure.

Principal Investigator:
Summer, D.A.

Objective:
To estimate demand function parameters for cigarettes and tobacco, focusing on taxes and prices for imported tobacco; simulate effects of policy changes; estimate supply function parameters and determinants of structure of tobacco farming industry.

Methods or Approach:
The economic theory of supply and demand will be applied at the farm and industry level. An econometric time series analysis of flexible demand systems will be made, as will descriptive multivariate analysis. A computer simulation of industry changes will be run.

Results to Date:
Elasticity of demand for cigarettes is approximately equal to -0.5 (United States). Elasticity of demand for U.S. tobacco is about -5.0. Imports are substitutable for U.S. tobacco in cigarettes. A large price decline in U.S. tobacco would encourage a relocation and expansion of the industry. Flue-cured tobacco farms are growing and tend to be as large as other farms. Burley farms are small and have not grown appreciably.

Project Dates:
1980–1987.

Financial Support:
North Carolina State University.

1320. RESEARCH TRIANGLE INSTITUTE, Cornwallis Road, Research Triangle Park, North Carolina 27709.

Project Title:
Chemical/Biological Analysis of Marijuana Smoke Condensate.

Principal Investigator:
Sparacino, C.M.

Objective:
To develop appropriate methodology (or use existing high-resolution methods) to analyze biologically active fractions of marijuana and tobacco smoke condensates.

Methods or Approach:
Marijuana (two types) and tobacco (one type) will be burned using two smoking conditions to produce six condensates, which will be fractionated via identical processes. The Ames/Salmonella assay will be applied to all crude material and fractions to assess mutagenic properties. Analytical method development will be directed toward fractions that are bioactive. Methods of analyzing the volatile and the nonvolatile portions of each active fraction will be applied (or developed). Where necessary, subfractionation using chromatographic techniques will be utilized. For characterization and comparison of marijuana and tobacco volatiles, gas chromatography/mass spectrometry will be the principal method. For the nonvolatile (heretofore uncharacterized) constituents, liquid chromatography/mass spectrometry is proposed. The development of radially compressed, micro-bore packed liquid chromatography systems is a goal of this project.

Results to Date:
The basic fractions of both marijuana smoke and tobacco smoke condensate (MSC and TSC) were the most mutagenic, with TSC bases testing as less mutagenic than either high- or low-potency marijuana MSC. Mutagenicity was detected in fractions where no mutagenicity was noted in crude condensates. Mutagenic activity required S9 activation. High resolution chromatography (GC, HPLC) has been conducted on active fractions. Development of radially compressed, flexible walled micro HPLC columns has been initiated.

Project Dates:
July 1983–June 1985.

Financial Support:
NIDA (R01-DA03417).

1321. USDA, AGRICULTURAL RESEARCH SERVICE, OXFORD TOBACCO RESEARCH LABORATORY, Route 2, Box 16G, Oxford, North Carolina 27565.

Project Title:
Genetics and Breeding of Polyphenols and Catechol in Tobacco.

Principal Investigators:
Gwynn, G.R.; Williamson, R.E.; Schlotzhauer, W.S.

Objective:
To (1) survey available tobacco germ plasm and identify sources that are low in total polyphenols, chlorogenic acid, rutin, catechol, and related chemicals; (2) hybridize identified chemicals with flue-cured tobacco cultivars; (3) study the pattern of inheritance; (4) select appropriate material within segregating populations to obtain lower total polyphenol, chlorogenic acid, and catechol; (5) determine the effects of different years and locations on chemical production; and (6) investigate the feasibility of using near infrared spectrometry to measure phenols.

Methods or Approach:
Previous studies that measured polyphenols using colormetric techniques provided information for selecting a group of test entries. Entries were grown at several locations in 1981 and 1982 under flue-cured cultural conditions. Cured samples were analyzed for total polyphenols, chlorogenic acid, rutin, and scopoletin. Pyrolysis of like samples provide chromatographic determinations for various phenols and phenol-related chemicals such as catechol. Genetic analysis is also being made of seven populations of low-phenol parents crossed with a standard flue-cured cultivar.

Results to Date:
Although findings are still incomplete, it has been determined that (1) some entries appear to be consistently lower than the flue-cured check in total polyphenols and chlorogenic acid; (2) phenol levels vary with locations and years; and (3) the lowest entries are usually either turkish or burley types.

Financial Support:
USDA, Oxford Tobacco Research Laboratory.

1322. UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL, HEALTH SERVICES RESEARCH CENTER, Chase Hall 132A, Chapel Hill, North Carolina 27514.

Project Title:
Effectiveness of Self-Help Smoking Cessation Strategies.

Principal Investigators:
Schoenbach, V.J.; Orleans, C.T.; Wagner, E.H., et al.

Objective:
To (1) develop three cost-effective self-help approaches to smoking cessation; (2) evaluate approaches in a large randomized controlled trial among enrollees of the Group Health Cooperative of Puget Sound (the fourth largest health maintenance organization in the United States); (3) establish the value of a comprehensive mailed quitting guide; and (4) assess whether minimal therapist contact and bolstered natural social supports for quitting influence results of a written self-help guide.

Methods or Approach:
Prospective subjects will be recruited through the group's monthly magazine and referrals by group physicians and nurses. Subjects meeting inclusion criteria will receive a motivational letter, quit smoking pamphlet, bibliography of self-help manuals, baseline questionnaire, and consent form. Participants will be randomly assigned to (1) the American Lung Association's manual "A Lifetime of Freedom From Smoking" plus a new quitting procedure incorporating nicotine fading techniques; (2) same materials plus information sent to subject-identified supportive individuals on how to provide more effect support to the prospective quitter; (3) same materials the second group receives plus four telephone calls from a counselor; or (4) nothing beyond initial letter, pamphlet, and bibliography. All materials will be sent through the mail. Followup of quit rates will be conducted by mailed questionnaires with telephone followup at 6, 12, 24, and 36 months. Salivary cotinine will be measured at 36 months for all self-reported quitters. Program effectiveness and factors important in the quitting process will be analyzed in relation to sex, age, source of referral, and smoking history. The study will provide a rigorous, long-term evaluation of three inexpensive, replicable self-help smoking cessation approaches.

Results to Date:
Project is in a preliminary phase.

Project Dates:
September 1984–continuing.

Financial Support:
NCI.

1323. UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL, Department of Maternal and Child Health, 407 Rosenau Hall, 201H, Chapel Hill, North Carolina 27514.

Project Title:
Mass Media and Prevention of Adolescent Smoking.

Principal Investigator:
Bauman, K.E.

Objective:
To evaluate long-term influence of mass media campaigns designed to prevent initiation of cigarette smoking by adolescents.

Methods or Approach:
Mass media campaigns, guided by behavioral science theory and the premise that they should be cost effective, focus on the consequences expected from smoking behavior and the stimulation of peer involvement. From Standard Metropolitan Statistical Areas (SMSAs) in the southeastern United States with fewer than 500,000 inhabitants, 10 will be randomly allocated to receive treatments that reflect increments in intensity and cost: (1) four control SMSAs will not receive the campaign; (2) two will receive radio messages that focus on selected expected consequences of smoking and not smoking; (3) two will receive radio messages plus a component to facilitate peer involvement; and (4) two will receive messages and peer involvement component via both radio and television. Baseline data will be collected from 223 adolescents and their mothers in each SMSA before the 6-month mass media campaign. Smoking behavior, expected consequences of that behavior, and antecedent and mediator variables will be measured. One year after the campaign, measures will be repeated with the same subjects. Interim measures for a subsample of 50 subjects in each SMSA will be taken within 1 month after the campaign to assess awareness and to provide estimates of early campaign effects. In addition to comparisons of experimental and control groups, and comparisons of experimental groups, analyses will determine if campaign effects vary according to mediating variables. Findings will be considered in the context of preventing onset of adolescent smoking.

Results to Date:
Project is in a preliminary phase.
Financial Support:
NCI (1R01CA38392-01).

1324. UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL, Box 1, 5034 Old Clinic Building, Chapel Hill, North Carolina 27514.

Project Title:
Study of Passive Smoking and Acute Middle Ear Effusions in Infants.

Principal Investigators:
Etzel, R.A.; Greenberg, R.A.; Henderson, F.W., et al.
Objective:
To examine the relationship between infant passive smoking and incidence of acute otitis media with effusion.
Methods or Approach:
Studies will be conducted on 139 children enrolled in the day care center at the Frank Porter Graham Child Development Center in Chapel Hill. Sera, drawn during the child's first year of life, will be analyzed for cotinine by radioimmunoassay. Children will be followed prospectively by a family nurse practitioner, who will record each episode and duration of acute otitis media with effusion in the child's first 3 years of life.
Results to Date:
Analyses of sera for cotinine were completed in January 1985.
Project Dates:
June 1983–June 1985.
Financial Support:
Robert Wood Johnson Foundation.

1325. UNIVERSITY OF NORTH CAROLINA, MOSES H. CONE MEMORIAL HOSPITAL, 1200 North Elm Street, Greensboro, North Carolina 27401-1020.

Project Title:
Control of Cigarette Smoking by Means of Hypnosis and Fading Procedure.

Principal Investigators:
Marshall, W.R.; Rothenberger, L.A.
Objective:
To empirically document the effectiveness of a 6-week therapy program aimed toward smoking reduction via hypnotic suggestion.
Methods or Approach:
Changes in cigarette butt length, number of cigarettes, tar intake, and nicotine intake were measured for nine subjects participating in a 6-week smoking reduction therapy program. Using repeated measure analysis, the points where statistically significant changed occurred were noted. A 1-month followup was conducted to determine any recidivistic effects.
Results to Date:
Subjects showed a significant improvement across the 6-week treatment period on all four criterion variables. Nicotine intake showed the greatest change, as subjects, on the average, decreased their nicotine from 25.4 mg (week 1) to 12.7 mg (week 6) for a 50 percent decrease ($F=7.954$; $p<0.001$). Tar intake decreased 45.3 percent from 310.5 mg in week 1 to 169.75 mg in week 6 ($F=39.53$; $p<0.001$). Subjects decreased the number of cigarettes smoked by 46 percent from 27.2/day in week 1 to 14.0/day in week 6 ($F=10.29$; $p<0.001$). Subjects also significantly altered the amount of cigarette smoked. The average butt length of the cigarettes in week 1 was 39.6 mm and increased to 43.7 mm by week 6 for a 9.8 percent change ($F=4.08$; $p<0.01$). At the 1-month followup, in terms of the number of cigarettes smoked, tar intake, and nicotine intake, the significant change remained from week 1 (baseline) to the followup session ($p<0.05$). The change in butt length, however, did not remain significant from week 1 to followup. The project has been completed and results have been submitted for publication.
Project Dates:
February 1978–1982.
Financial Support:
KTHRI.

1326. UNIVERSITY OF NORTH CAROLINA, SCHOOL OF NURSING, Carrington Hall 214H, Chapel Hill, North Carolina 27514.

Project Title:
Smoking Habits of Professional Nurses in North Carolina.

Principal Investigators:
Swenson, I.; Dalton, J.
Objective:
To analyze present smoking behavior, attempts to quit smoking or reduce consumption, and changes in habits over time of professional nurses in relation to selected factors.
Methods or Approach:
A cross-sectional questionnaire survey of a 5 percent random sample of registered nurses in North Carolina was conducted in 1981; 56 percent responded, giving a final sample of 601 (no followup was conducted to increase response rate). Information was provided on smoking habits (type and amount of cigarettes smoked, age when smoking started, attempts to quit or reduce consumption, years smoked, and situational factors that encouraged smoking). In addition, data were collected on selected socioeconomic and professional characteristics, attitudes and behaviors regarding antismoking efforts, role modeling attitudes, and peer and family influences.
Results to Date:
There were no significant differences by smoking status (current, former, or never smoker) in sociodemographic characteristics, professional characteristics (job setting, position), job satisfaction, or conditions of employment. Never smokers were less likely than ever smokers to have had peers who smoked in high school and nursing school. Although smokers were more likely than nonsmokers to have spouses and children who smoked, there were no differences by smoking status in the proportions who had parents that smoked. Former smokers had the strongest antismoking attitudes and engaged in more antismoking behavior than never or current smokers, although less than 10 percent of all nurses indicated involvement in antismoking education efforts. Nurses who successfully quit smoking more frequently indicated reasons related to their own health. Current smokers indicated reasons for continuing to smoke related to associations between cigarette smoking and social situations (meals, breaks), rather than stress-related situations.
Project Dates:
July 1980–July 1984.
Financial Support:
University of North Carolina, School of Nursing.

1327. UNIVERSITY OF NORTH CAROLINA, SCHOOL OF MEDICINE, Department of Pediatrics, Clinical Sciences Building 229H, Chapel Hill, North Carolina 27514.

Project Title:
Intervention Program to Reduce Passive Smoking by Infants.

Principal Investigator:
Loda, F.A.
Objective:
To reduce passive smoking by infants in the first year of life and thereby reduce frequency and/or severity of lower respiratory illnesses.
Methods or Approach:
All infants born during a 2-year period to families residing in a rural North Carolina county will be recruited for a randomized, controlled intervention study designed to decrease infants' exposure to tobacco smoke. The intervention group will receive a passive smoking reduction program and a general respiratory hygiene education program; the control group will receive only the respiratory hygiene program. Programs will be given by nurses who will visit the homes of the infants regularly during the first 6 months of life. Tobacco smoke exposure will be monitored by questionnaire and the infant's urine cotinine excretion. Respiratory illnesses among the infants will be monitored by diaries kept by the families. Data will be collected during the first year of life.
Results to Date:
Infants exposed to tobacco smoke absorb constituents, and urinary excretion of cotinine was found to be a reliable measure of such exposure in infants. It was also found that infants exposed to tobacco smoke products in utero excrete cotinine in urine during the first days of life.
Future Plans:
Future research will (1) establish a cohort of infants and their households suitable for studying the natural history of chronic respiratory disease; and (2) establish a geographically defined community for future study of the effectiveness of other techniques for reducing risk of respiratory illness.
Project Dates:
September 1984–September 1989.
Financial Support:
NHLBI (1R18HL28895-01).
Reference:
Greenberg, R.A.; Haley, N.J.; Etzel, R.A., et al. "Measuring the Exposure of Infants to Tobacco Smoke: Nicotine and Cotinine in Urine and Saliva." *New England Journal of Medicine* 310(17):1076-1078, April 26, 1984.

1328. USDA, AGRICULTURAL RESEARCH SERVICE, Oxford, North Carolina 27565.

Project Title:
Improved Tobacco Safety by Engineering Aspects of Pest Control and Harvest-Curing Methods.

Principal Investigator:
Lam, J.J., Jr.
Objective:
To (1) improve tobacco safety by conceiving, designing, testing, and evaluating methods and systems to reduce pesticide requirements and residues in leaf and soil; (2) reduce or eliminate hazardous constituents by new harvest and curing processes; and (3) remove protein from tobacco for human and animal consumption.
Methods or Approach:
The program will (1) rear and release 500,000 or more pest egg-predators *Jalysus spinosus* each early spring to augment native populations in a countywide experiment; (2) develop improved mass-rearing procedures for *J. spinosus, Compoletis sonorensis,* and other beneficial insects; (3) design and evaluate insect traps and/or attractants; (4) develop and evaluate equipment and procedures in experimental homogenized leaf curing (HLC) system to reduce or eliminate components that may be related to health; (5) measure and describe physical properties and boundaries in each process stage; (6) automatically control product improvements; (7) provide sheet for local evaluation and biological tests; and (8) remove and dry high-grade protein.
Results to Date:
About 200,000 adult stilt bugs were reared on greenhouse tobacco during winter months for marking and releasing during May and June. Several marking methods were tested. Five separate releases were made by entomologists to determine movement and distribution patterns of the insects. Several categories of tobacco were processed in the HLC/protein pilot plant. Tobacco, harvested at Whiteville, N.C., in a green state, was used in extended protein removal tests. Green fibers were treated in a variety of ways as a silage for possible animal feed. Tobacco at Oxford, N.C., harvested at various stages of maturity, was homogenized, fractionated, and recombined in various ways to isolate undesirable components. Separated fractions were also heat treated at several process stages. Nonfractionated tobacco slurry was sparged with several rates and temperatures of air during curing periods. Six reactors were designed and constructed for use in a series of ozone treatments of tobacco slurry.
Project Dates:
April 1979–May 1984.
Financial Support:
USDA (6647-20883-001D).
References:
(1) Lam, J.J., Jr.; Baumhover, A.H. "Nocturnal Response of *Heliothis virescens* to Artificial Light and Sex Pheromones." *Environmental Entomology* 11:1032-1035, 1982. (2) Lam, J.J., Jr.; Elsey, K.D.; Baumhover, A.H. "Mass Rearing of *Jalysus spinosus*, an Insect Predator on Greenhouse Tobacco." *Environmental Entomology* (In Press). (3) Schepartz, A.I.; Mottola, A.C.; Scholtzhauer, W.S., et al. "Effect of Ozone Treatment of Tobacco on Leaf Lipids and Some PAH: A Pilot-Plant Trial." *Tobacco Science* 25:120-122, 1982.

1329. USDA, AGRICULTURE RESEARCH SERVICE, Oxford, North Carolina 27565.

Project Title:
Improve Tobacco Safety by Altering Chemical and Physical Factors of Leaf.

Principal Investigators:
Williamson, R.E.; Rufty, T.W.
Objective:
To (1) study biochemical properties of tobacco grown and processed by different methods; (2) analyze relationship of enzyme activities and concentrations of chemical components during plant development, leaf senescence, and curing to understand how to regulate formation and accumulation of naturally occurring substances that are health related; (3) determine organic and inorganic constituents (including protein) in connection with culture, fertility, processing, curing, breeding, and physiological studies to reduce or eliminate harmful constituents; and (4) develop or improve analyses to measure health-related chemical constituents.

Methods or Approach:
The following analyses for polycyclic aromatic hydrocarbons (PAHs) on smoke condensate of HLC tobacco were conducted: fibers only, fibers plus protein, fibers plus deproteinized (depro) juice, and fibers plus protein plus depro juice. PAHs were lowest when fractions (fibers, protein, depro juice) were recombined. Drying conditions of HLC slurry changed alkaloid levels and physical quality, and affected smoke nitrosonornicotine. Nutritional tests show that HLC depro fibers were too low in nondetergent fibers. A method was developed to assay activities of enzymes involved in coumarin biosynthesis. Freeze-dried ground tobacco was exposed to yellowing temperature for 0 to 48 hours in presence of air and nitrogen gas (N_2) and analyzed for polyphenols, sugars, and starch. Polyphenols ranged from 1.1 to 3.9 percent and increased from first to last harvest. Polyphenols were lower in presence of N_2. No starch conversion took place in N_2 atmosphere. After 48 hours in N_2, sugar content was unchanged.. After yellowing tobacco leaves for 48 hours, barn temperature was increased to 60° C in 1 hour and then lowered to 35° C in 1 hour to brown leaf. Temperature was then programmed for normal curing. Samples were analyzed for alpha-amino N, total nitrogen (TN), acid-insoluble N, NO_3, ash, alkalinity of water-soluble ash, starch, sugars, and polyphenols.

Results to Date:
Levels of alpha-amino N, TN, NO_3, and ash were the same in treated and control samples. Level of acid-insoluble N was lower for treated than for control (1.25 vs. 1.15 percent) samples. Level of water-soluble ash was higher for treated samples (3.5 vs. 4.5 percent).

Project Dates:
October 1979–October 1984.

Financial Support:
ARS (6647-20881-010D).

References:
(1) Williamson, R.E.; Gwynn, G.R. "Varieties of Polyphenols in Flue-Cured Tobacco Cultivars Attributed to Location, Stalk Position, and Year." *Crop Science* 22:144-146, 1982. (2) McClure, W.R.; Williamson, R.E. "Rapid Spectrophotometric Analysis of the Chemical Composition of Tobacco. III. Polyphenols." *Beitraege zur Tabakforschung International* 11:219-227, 1982. (3) Schlotzhauer, W.S.; Martin, R.M.; Snook, M.E., et al. "Pyrolytic Studies on the Contribution of Tobacco Leaf Constituents to the Formation of Smoke Catechols." *Journal of Agriculture and Food Chemistry* 30:372-374, 1982.

1330. USDA, ARS, NORTH CAROLINA STATE UNIVERSITY, Raleigh, North Carolina 27650.

Project Title:
Analytical Evaluation of Low PMI Tobaccos.

Principal Investigator:
Weeks, W.W.

Objective:
To expand chemical evaluation of low particulate (PMI) tobaccos through evaluation of volatile and lipid constituents; further increase knowledge of flavor and aroma associated with low-tar tobacco.

Methods or Approach:
Contrasting low PMI tobaccos and standard flue-cured varieties will be analyzed for several classes of compounds, volatile and nonvolatile. Investigations will involve stem distillation and solvent partitioning of low PMI and standard flue-cured tobaccos to elucidate favorable or unfavorable quality associated with flavor and aroma.

Results to Date:
Selection and breeding of flue-cured tobacco to reduce particulate matter and tar have resulted in a 14 percent decrease in particulate matter. Tobaccos grown at two locations after 7 years of selection were also 10 percent lower in volatile compounds and 8 percent lower in long chain fatty acids than the original plant population at each location. Other experiments were conducted to monitor changes in the leaf chemistry and to alter PMI. A factorial experiment with two soils, three nitrogen levels, three moisture regimes, and two different tillages determined effect of management on volatile components in tobacco. Sixty-five compounds were quantified, and significant differences associated with a particular management variable were measured, including soils 39, nitrogen 37, moisture 19, and tillage 13. Results indicate that management of flue-cured tobacco is important to tobacco aroma. Leaves were allowed to develop on only one-third of tobacco plants to determine if the chemistry of the leaf could be modified selectively. Lower leaves in each case were similar to bottom leaves if they were from the lower, middle, or upper one-third of the plant. Higher alkaloid levels than normal were obtained from all plants because of the abnormal shoot:root ratio. Curing tobacco from lower and upper primings indicated that most of the volatile compounds found in flue-cured tobacco are formed following yellowing.

Project Dates:
October 1978–September 1983.

Financial Support:
USDA (NC03629).

Reference:
Chang, K.W. "I. Changes in the Surface Chemistry of Tobacco Leaves During Curing With Particular Emphasis on Trichomes. II. Changes in Volatile Oils of Flue-Cured Tobacco During Curing." Doctoral Dissertation, North Carolina State University, Raleigh, 1983, 96 pp.

1331. USDA, ARS, TOBACCO RESEARCH LABORATORY, Oxford, North Carolina 27565.

Project Title:
Improve Tobacco Safety by Genetic Principles and Practices.

Principal Investigators:
Chaplin, J.F.; Sisson, V.A.; Gwynn, G.R.

Objective:
To reduce or eliminate constituents in tobacco that are harmful to health by genetic principles; reduce or eliminate harmful exogenous chemical residues in tobacco leaf and smoke by developing germplasm resistant to pests.

Methods or Approach:
Comprehensive genetic programs, including evaluation of germplasm and intra- and interspecific transfer of desirable factors that control constituents important to smoking and health (such as nicotine and tar) will be conducted. New techniques will be developed using the latest genetic techniques (e.g. haploid–diploid method, interspecific gene transfer). Conventional and new methods for developing pest-resistant genotypes will be used to study effects of transferred factors on morphological and physical characteristics of the plant.

Results to Date:
Tobacco Introductions (TI) having reduced levels of particulate matter were grown (PMI values ranged from 172 to 231 mg/g). TIs will be used for long-term population improvement to reduce tar. Lines of flue-cured tobacco with different levels of total alkaloids (TA) were developed and evaluated for agronomic, chemical, and smoke parameters. Levels obtained were NC 95 family, 0.34, 1.08, 2.05, 3.11, and 3.55 percent; SC

58 family, 0.38, 1.59, 1.90, 2.82, 4.18, and 4.82 percent; and Coker 139 family, 0.20, 0.93, 1.66, 1.84, and 2.17 percent. High TA lines were lower in yield and in most families gave highest grade index. Smoke pH increased with TA levels. Smoke was evaluated by two panels; panel A showed differences due to alkaloid levels, and panel B showed that increases in TA were accompanied by increased smoke flavor, a major accomplishment, since previous brown spot lines from Beinhart 1000-1 produced off-flavor. Recurrent selection within a population for reducing polyphenols was continued. In cycle 2, mean of all lines was 16 percent lower than low percent Sp G-28; in cycle 3, lines used were below Sp G-28. Levels and composition of leaf cuticular components as a function of plant age and fate during curing were determined. Lowest levels of cuticular components were found on plant bed leaves and highest at 10 weeks.

Project Dates:
October 1979–October 1984.

Financial Support:
USDA (6647-20881-011D).

References:
(1) Burk, L.G.; Gooding, G.V.; Chaplin, J.F. "Reaction of *Nicotiana* Species and Cultivars or Breeding Lines of *Nicotiana tabacum* to Three Strains of Potato Virus Y." *Tobacco Science* 26:85-88, 1982. (2) Campbell, C.R.; Chaplin, J.F.; Johnson, W.H.H. "Cultural Factors Affecting Yield, Alkaloids, and Sugars of Close-Grown Tobacco." *Agriculture Journal* 74:279-283, 1982. (3) Campbell, J.S.; Chaplin, J.F.; Boyette, D.M., et al. "Effect of Plant Spacings, Topping Heights, N Rates and Varieties of Tobacco on Nicotine Yield and Concentration." *Tobacco Science* 26:66-69, 1982.

1332. VETERANS ADMINISTRATION MEDICAL CENTER, 2500 Erwin Road, Durham, North Carolina 27705.

Project Title:
Health Locus of Control and Smoking After CABG Surgery.

Principal Investigators:
Coyle, M.; Munster, M.

Objective:
To investigate the relationship between internal-external health locus of control and compliance to smoking cessation after coronary artery bypass graft (CABG) surgery.

Methods or Approach:
The research design for this nonexperimental study uses a cross-sectional survey approach. Data will be collected from nonrandom sampling of post-CABG surgery patients attending the Durham Veterans Administration Hospital Cardiology Clinic. Data collection, requiring about 20 minutes, will be conducted during the regularly scheduled clinic visit. A self-administered questionnaire will be used to measure demographic variables and locus of control (Wallston's Health Locus of Control Scale).

Results to Date:
Project is in a preliminary phase.

Financial Support:
VA.

1333. VETERANS ADMINISTRATION MEDICAL CENTER, 2500 Erwin Road, Durham, North Carolina 27705.

Project Title:
Survey of IGA Responses in Sputum and Serum of Surgical Patients.

Principal Investigator:
Wolfe, W.G.

Objective:
To analyze the secretory immune response to bronchogenic cancer of the lung.

Methods or Approach:
Level of immunogloblin A (IgA) and its associated secretory component (SC) were measured in bronchial secretions of patients with lung cancer and comparisons were made to patients with nonmalignant disease. The predictive value of these measurements in case of lung cancer and their use as a screening modality in high-risk patients was evaluated. Studies were extended to include tumors arising on mucous surfaces in the oral and pharyngeal regions. Studies included levels of secretory IgA (SIgA) in serum samples. Serum was collected from 52 individuals in order to define each category according to smoker/nonsmoker and according to the type of benign or malignant disease. Serum was collected on individuals at different stages of treatment to determine the prognostic value of SIgA levels. IgA and SC levels in serum were similarly studied.

Results to Date:
The role of the secretory immune system in bronchogenic carcinoma and other epithelial malignancies has been established. There was a substantial difference in the SIgA levels between normal and cancer patients, including lung, head, and neck malignancies. IgA appeared to be elevated in patients with epithelial tumors, and secretory components could be measured in elevated quantities in plasma of patients with epithelial malignancies including breast and ovarian cancer. Fifty-two patients were studied with no untoward effects. The present studies have been completed, and results are being prepared for publication.

Financial Support:
VA.

1334. VETERANS ADMINISTRATION MEDICAL CENTER, 2500 Erwin Road, Durham, North Carolina 27705.

Project Title:
Predicting Initiation of Attempts to Stop Smoking—II.

Principal Investigator:
Shipley, R.H.

Objective:
To determine the role of individual differences in the initiation of attempts to quit or reduce smoking.

Methods or Approach:
Smokers visiting the 1982 Durham Health Fair were asked to participate. Volunteers completed several questionnaires (personality and smoking), read antismoking materials, and were called 1 and 3 months later to assess smoking changes. No veteran patients participated.

Results to Date:
The degree of change in the smoking of participants was too small to allow prediction of results based on individual differences.

Financial Support:
VA.

1335. VETERANS ADMINISTRATION MEDICAL CENTER, 2500 Erwin Road, Durham, North Carolina 27705.

Project Title:
Predicting Initiation of Attempts to Stop Smoking.

Principal Investigator:
Shipley, R.H.
Objective:
To test an alternative theory of smoking reduction incorporating three distinct stages: initial decision, initial control, and maintenance.
Methods or Approach:
Three measures (perceived health locus of control, desire to stop, and self-esteem) were used to predict self-initiated smoking reduction in 61 regular smokers. Criterion smoking change measures (one for each stage) were obtained at followup.
Results to Date:
Multiple regression analyses of the criteria showed that a different set of predictors were significant for each: desire to stop predicted the decision of reduce smoking, self-esteem predicted initial smoking reduction, and the combination of internal health locus of control beliefs and strong desire to stop predicted successful maintenance of reduction. The differential success across criteria of the predictors shows the value of the stage analysis and suggests the development of smoking treatments varying by stage.
Financial Support:
VA.

1336. VETERANS ADMINISTRATION MEDICAL CENTER, 2500 Erwin Road, Durham, North Carolina 27705.

Project Title:
Smoking Control.

Principal Investigator:
Shipley, R.H.
Objective:
To determine effects of smoking control programs.
Methods or Approach:
In study 1, 42 smoking subjects received either bogus psychological test feedback suggesting high potential for maintaining abstinence or neutral feedback and subliminal stimulation with either a supportive or a neutral message relative to abstinence. In study 2, 45 subjects attended a smoking treatment program designed to produce either abstinence or a reduced level of smoking. In study 3, 33 people who have published controlled smoking-cessation articles were surveyed regarding the measurement, practices, and conventions they used in their research.
Results to Date:
Study 1 is at present in a data analysis phase. Findings of study 2 indicate that overall success in reducing smoking and carbon monoxide levels was superior in the group whose goal was abstinence. Twenty-five responses were received in study 3. No adverse affects were noted as a result of any of the three research protocols.
Financial Support:
VA.
Reference:
Shipley, R.H.; Rosen, T.J.; Williams, C. "Measurement of Smoking: Surveys and Some Recommendations." *Addictive Behaviors* 7(3):299-302, 1982.

1337. VETERANS ADMINISTRATION MEDICAL CENTER, 2500 Erwin Road, Durham, North Carolina 27705.

Project Title:
Smoking Treatment—Achieving and Maintaining Abstinence.

Principal Investigator:
Shipley, R.H.
Objective:
To assess the effectiveness of supportive maintenance letters in helping subjects achieve and maintain smoking abstinence.
Methods or Approach:
Following smoking-cessation treatment, half of 44 subjects were sent supportive maintenance letters.
Results to Date:
No adverse effects resulting from the research protocol were noted. Letters produced no main effect but reduced smoking in subjects who smoked from habit or who received little pleasure from the sensorimotor stimulation of smoking, perhaps by increasing their awareness of smoking. Letters also reduced smoking in subjects with high muscle tension. Letters increased smoking among opposite subject groups and in those believing powerful others could not influence their health. Independent of letter receipt, maintenance was enhanced by internal health locus of control and hampered by chance control expectancies.
Financial Support:
VA.
Reference:
Shipley, R.H., "Maintenance of Smoking Cessation: Effect of Follow-Up Letters, Smoking Motivation, Muscle Tension, and Health Locus of Control." *Journal of Consulting and Clinical Psychology* 49:982-984, 1981.

North Dakota

1338. NORTH DAKOTA STATE DEPARTMENT OF HEALTH, State Capitol, Judicial Wing, Bismarck, North Dakota 58505.

Project Title:
Telephone Risk Factor Prevalence Survey.

Principal Investigators:
Wentz, R.; Campbell, P.; Monteith, D., et al.
Objective:
To develop estimates of behavioral risk factor prevalence in North Dakota's population and to monitor progress toward the goals of risk reduction.
Methods or Approach:
Telephone interviews of randomly selected households were conducted, using a standard questionnaire. Information was obtained on smoking, exercise, alcohol misuse (including drinking and driving), obesity, hypertension, stress, and seat belt use. Basic demographic data were also requested.
Results to Date:
Results show that the proportion of the population ($\geq$ 18 years of age) at risk to be (1) 64.3 percent for seat belt use; (2) 26.9 percent, smoking; (3) 25.6 percent, obesity; (4) 24.0 percent, acute drinking; (5) 19.7 percent, sedentary lifestyle; (6) 13.4 percent, chronic heavy drinking; (7) 6.8 percent, drinking drivers; and (8) 1.1 percent, uncontrolled hypertension.

Future Plans:
A behavioral risk factor surveillance system, an extension of the telephone survey, will be initiated in 1985.
Project Dates:
February 1984–November 1984.
Financial Support:
CDC; North Dakota State Department of Health.

1339. NORTH DAKOTA STATE UNIVERSITY, OREGON RESEARCH INSTITUTE, Department of Psychology, Programs in Health and Behavior, Fargo, North Dakota 58102.

Project Title:
Competition-Based Worksite Smoking Interventions.

Principal Investigators:
Klesges, R.C.; Glasgow, R.E.
Objective:
To evaluate effectiveness of worksite smoking reduction/cessation program with/without formal competition; test incremental effects of personal incentives on participation and success rates.
Methods or Approach:
Participants (n=107) from four banking institutions and one savings and loan received a standardized smoking cessation/reduction program. The banks also participated in a competition in which the bank with the most successful outcome received monetary and other prizes.
Results to Date:
Data indicate that significantly more subjects in the competition condition participated than in the noncompetition condition (88 percent vs. 53 percent). Despite the higher participation rate and higher levels of nicotine addiction in the competition condition, subjects were as successful in reducing smoking as subjects in the noncompetition condition. At posttest, 23 percent of subjects were confirmed abstinent by carbon monoxide and thiocyanate testing, with no differences between institutions or conditions. Among nonabstinent subjects, an overall reduction of 51 percent was achieved in carbon monoxide levels. At 6-month followup, subjects in the competition condition had significantly lower levels of carbon monoxide than subjects in the noncompetition condition.
Future Plans:
Followup assessments will continue to evaluate long-term effectiveness of the competition-based program. In addition, full-scale controlled replications are underway in a variety of worksite settings to evaluate the generalizability of the program.
Project Dates:
August 1983–July 1985.
Financial Support:
NHLBI (HL 30615).

1340. NORTH DAKOTA STATE UNIVERSITY, COLLEGE OF PHARMACY, Department of Pharmaceutical Sciences and Toxicology, Fargo, North Dakota 58105.

Project Title:
Interaction Between Phencyclidine and Its Smoking Product, 1-Phenylcyclohexene.

Principal Investigator:
Chaturvedi, A.K.
Objective:
To evaluate the mechanism of interaction between phencyclidine and its pyrolysis product 1-phenylcyclohexene, including toxicological evaluation of the pyrolysis product.
Methods or Approach:
Animals were administered appropriate doses of 1-phenylcyclohexene by oral intubation daily for up to 7 days. On certain days, animals were challenged with phencyclidine and changes in behavior, compared with controls (challenged with corn oil) were noted. Liver toxicity was compared using various parameters. Effect of the pyrolysis product on translocation of phencyclidine is being studied.
Results to Date:
It appears that 1-phenylcyclohexene treatment for 7 days produces some undesirable effects on mouse liver function that are reversible on discontinuation of treatment. 1-Phenylcyclohexene also weakens toxic effects of phencyclidine; however, the mechanism by which 1-phenylcyclohexene exerts its effects has yet to be established.
Project Dates:
January 1982–December 1986.
Financial Support:
North Dakota State University.

Ohio

1341. 3205 PLAINVIEW, Toledo, Ohio 43615.

Project Title:
Changes in Smoking Habits Among Junior High School Students. Third Follow Up.

Principal Investigators:
Pullella, J.L.; Kelson, S.R.
Objective:
To (1) survey smoking habits of students in grades 7 through 12 in Toledo and Lucas County (Ohio) public schools; (2) determine prevalence of smoking; (3) determine reasons for smoking or not smoking and for smoking by other students; (4) determine students' beliefs about health hazards of smoking; (5) establish smoking habits of parents; (6) elicit views of students as to parents' attitude toward students' smoking; (7) determine whether students smoke in presence of parents; and (8) establish influence of television and radio programs on students' ideas about smoking.
Methods or Approach:
Approximately 20,000 students were surveyed. Forms were distributed to school principals, and teachers were provided with instructions on how to conduct the survey. Agencies cooperating included American Cancer Society, Toledo and Lucas County Health Departments, Northwest Ohio Heart Association, University of Toledo, Medical College of Ohio, Northwest Ohio Lung Association, and Toledo and Lucas County Boards of Education. A fourth survey was conducted in 1983 and results are being tabulated. In connection with the survey, a control study was carried out in two large high schools to determine if smoking education has a beneficial effect. In one school, antismoking education was given after a

presurvey. In the other school, no education was given. A postsurvey was conducted in both schools.

Results to Date:
Smoking in schools is of epidemic proportions. From 1961 to 1971, smoking by boys and girls increased at every grade level. More boys reported smoking in all grades except in grades eight and nine in 1971, when the percentage of girls who smoked exceeded the percentage of boys who reported smoking. In 1976, there was an increase in every grade in the percentage of girl smokers (nearly double in grade seven). For boys, smoking had increased in grades 7, 8, and 9 (over 1971) but had decreased in grades 10, 11, and 12. In 1976, girls exceeded boys not only in grades 8 and 9 as in 1971, but in every other grade surveyed except grade 12.

Future Plans:
A fourth survey was conducted in 1983 and results are being tabulated.

Project Dates:
June 1983–September 1985.

Financial Support:
ACS; Northwest Ohio Heart Association; Northwest Ohio Lung Association; University of Toledo, College of Pharmacy; Blue Cross of Northwest Ohio.

Reference:
Kelson, S.R.; Pullella, J.L.; Fulton, G.B. "The Control of Smoking: The Physician's Role." *Ohio State Medical Journal* 76(6):359-362, June 1980.

1342. AMBERLEY ASSOCIATES, P.O. Box 36236, Cincinnati, Ohio 45236.

Project Title:
SMOKEBUSTERS: A One Hour Documentary Film on the Effects of Ambient Tobacco Smoke on Nonsmokers and the Impact of Nonsmokers' Rights Groups on the Legislative Process.

Principal Investigator:
Leichtman, A.P.

Objective:
To provide a national view of the impact of nonsmokers' rights groups on the legislative process at the national, state, and local level.

Methods or Approach:
Input is being sought from 37 national, state, and local groups, the U.S. Department of Health and Human Services, and consulting firms. The 1985 hearings on passive smoking by the Cincinnati City Council and city Board of Health will provide a test arena to study the decisionmaking process, previous guidelines that called for voluntary compliance, the Board of Health's Strategic Planning Committee's examination of passive smoking, and the mandate it has been given by the city government to implement guidelines established more than a decade ago. In addition, a public opinion survey on the impact of the proposed guidelines on city employees is being conducted to investigate enforcement, probability of problems in ventilation, employee morale, and economic and health impacts. Information is also being sought on the current status of state and local legislation, economic impact, health costs, reasons for lack of willingness of media to research the subject area, impact of organized groups on the legislative process, national coordination of nonsmokers' rights movement, opposition of the Tobacco Institute and others, status of research on passive smoking and its impact on public opinion, and prospects for governmental intervention.

Results to Date:
Project is in a preliminary phase.

Future Plans:
It is hoped that the film will get prime-time national television exposure and/or syndication to national, state, and local community agencies interested in the problems of passive smoking.

Project Dates:
June 1984–December 1985.

Financial Support:
Amberley Associates.

1343. BOWLING GREEN STATE UNIVERSITY, ELECTRON MICROSCOPY CENTER, Bowling Green, Ohio 43403.

Project Title:
Structure, Interrelationships, and Chemical Identity of Spicules in Rat Lung Following Chronic Tobacco Smoke Exposure.

Principal Investigators:
Heckman, C.A.; Anderhalt, R.

Objective:
To determine number of structural classes represented by intracellular spicules related to tobacco smoke exposure; determine whether the particles undergo dose-dependent changes in size or shape (indicating that they develop in situ over the course of chronic smoke exposure).

Methods or Approach:
Classification of spicule-like particles by size and shape will be conducted after serial reconstruction of a large number of specimens from their ultrastructural appearance in thin sections. The repeating order (if any) of the inclusions will be determined by electron diffraction conducted at varying degrees of tilt in the electron microscope. The elemental composition of the spicules will be estimated by x-ray energy dispersive spectrometry and electron energy loss spectrometry.

Results to Date:
The elemental composition of intracellular spicules in the lung, estimated by x ray energy dispersive analysis, seems to indicate that they may originate within the cells themselves. The ultrastructure and distribution of intracellular spicules in tobacco smoke-exposed rats has already been describe'

Future Plans:
Characteristics of intracellular inclusions in the human lung will be investigated and particles extracted from tobacco smoke condensate will be studied to see whether they bear any resemblance to the intracellular spicules.

Project Dates:
June 1984–June 1987.

Financial Support:
Bowling Green State University; NIH (RR03123-04).

Reference:
Heckman, C.A.; Lehman, G.L. "Ultrastructure and Distribution of Intracellular Spicules in Rat Lung Following Chronic Tobacco Smoke Exposure." *Journal of the National Cancer Institute* (In press).

1344. CASE WESTERN RESERVE UNIVERSITY, CLEVELAND METROPOLITAN GENERAL HOSPITAL, 3395 Scranton Road, Cleveland, Ohio 44109.

Project Title:
Effects on the Developing Child of Fetal Exposure to Maternal Smoking, Alcohol Use, and Lead Exposure.

Principal Investigators:
Ernhart, C.B.; Wolk, A.W.; Sokol, R.J., et al.

Objective:
To determine the extent to which the child's development is influenced by a maternal history of alcohol abuse, alcohol use in pregnancy, smoking in pregnancy, and low level lead exposure.

Methods or Approach:
The research sample consists of a cohort of 359 low SES infants delivered to women studied during the prenatal period. Independent variables are maternal score on Michigan Alcoholism Screen Test, average ounces alcohol/day, cigarettes smoked/day, and serum thiocyanate levels. Maternal and cord blood levels were related to these factors and are also related to outcome measures. Children are being assessed with appropriate measures during the preschool period. Relevant associated measures are being obtained for covariate entry into statistical models.

Results to Date:
Alcohol use and smoking in pregnancy were related in a dose–response manner to maternal blood lead level and to cord blood lead level. Maternal alcohol use in pregnancy was related to occurrence of neonatal anomalies.

Future Plans:
Data analysis is underway to assess the effects of each factor on neonatal status and on relevant outcome measures during infancy. The cohort will be followed through age 4 years, 9 months with measures selected on the basis of sensitivity to developmental deficit. Appropriate analysis of the longitudinal dataset is being developed.

Project Dates:
January 1981–June 1988.

Financial Support:
NICHHD (HD 14883); March of Dimes Birth Defects Foundation; International Lead Zinc Research Organization, Inc.

1345. CASE WESTERN RESERVE UNIVERSITY, CLEVELAND METROPOLITAN GENERAL HOSPITAL, Department of Obstetrics and Gynecology, 3395 Scranton Road, Cleveland, Ohio 44109.

Project Title:
Interaction Between Cadmium and Zinc in Pregnant Women Who Smoke.

Principal Investigators:
Kuhnert, P.M.; Kuhnert, B.R.

Objective:
To test the hypothesis that the increased cadmium (Cd) level in pregnant women who smoke alters metabolism of zinc in the maternal-fetal placental unit, which may contribute to lower birth weight infants.

Methods or Approach:
The interaction of Cd with the essential nutrient zinc is well established in pregnant animals, but no similar studies have been conducted on pregnant humans. Zinc status of mothers and infants will be evaluated using plasma and red cell zinc levels and serum alkaline phosphatase activity. Levels of zinc and alkaline phosphatase will also be measured in the placenta. Cd exposure will be evaluated by determining levels of Cd in maternal blood and placental tissue, and by determining metallothionein levels in the placenta. To evaluate whether Cd exposure due to smoking affects zinc metabolism, various biochemical and clinical parameters of two population groups (smokers and nonsmokers) will be compared. Serum thiocyanate levels will be used to classify patients as smokers or nonsmokers.

Results to Date:
Although more patients are needed before statistical analysis is appropriate, the following trends have been noted in the 21 primiparous and 68 multiparous women and their infants studied to date: (1) mean levels of Cd in maternal blood and placental tissue of pregnant women who smoke are higher than levels in nonsmokers; (2) mean plasma and red blood cell levels of zinc in maternal blood and cord blood of smokers is lower than levels in nonsmokers; (3) placental zinc levels appear to be higher in smokers; (4) total and heat-sensitive fractions of alkaline phosphatase are elevated in smokers; and (4) higher levels of metallothionein are found in placentas of smokers. Plasma thiocyanate levels are being used successfully to help distinguish smokers from nonsmokers. Preliminary analysis using multiple correlation analysis and regression analysis suggest that there is an interaction between Cd exposure and zinc status.

Project Dates:
September 1982–May 1987.

Financial Support:
NICHHD (5MO1RR00210; R01HD17015).

1346. CASE WESTERN RESERVE UNIVERSITY, SCHOOL OF MEDICINE, Department of Reproductive Biology, Cleveland, Ohio 44106.

Project Title:
Multiple Mixed-Function Oxidases of the Human Placenta.

Principal Investigator:
Meigs, R.A.

Objective:
To discriminate, characterize, and isolate mixed-function oxidases of the human placenta that are responsible for synthesis and metabolism of estrogens and other steroid hormones and for transformation of exogenous xenobiotic chemicals such as drugs and carcinogenic hydrocarbons.

Methods or Approach:
Kinetic studies with competitive inhibitors and other active-site directed inhibitors ("suicide substrates") will be used to characterize and differentiate substrate binding sites of individual oxidase systems. Effector action of steroids, hemoprotein ligands, and xenobiotic chemicals such as drugs and environmental pollutants will be similarly evaluated by kinetic means to further characterize and differentiate the various oxidase activities of the placenta. The selective inductive stimulus of maternal smoking on individual placental oxidase activities will also be utilized as a discriminatory factor. Physical validation of the existence of discrete oxidase proteins will be pursued by solubilization, fractionation, purification, and characterization of components of the native membranous mixed-function oxidase systems.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Results will be used in future research to clarify the relationship of estrogens, carcinogen hydrocarbons, and other aromatic chemicals as substrates, inducers, and effectors of mixed-function oxidase activities and their roles in normal and abnormal placental function.

Project Dates:
September 1984–August 1987.

Financial Support:
NICHHD (HD19258).

1347. CASE WESTERN RESERVE UNIVERSITY, SCHOOL OF MEDICINE, 2119 Abington Road, Cleveland, Ohio 44106.

Project Title:
Role of Ethanol in the Etiology of Head and Neck Cancer.

Principal Investigator:
McCoy, G.D.
Objective:
To (1) determine the effect of alcohol consumption on metabolism of tobacco-associated carcinogens by target tissues, N'-nitroso-nornicotine (NNN), N-nitrosopyrrolidine (NYPR), and benzo(*a*)pyrene (BaP) in trachea, BaP in lung, and NPYR and BaP in oral cavity; (2) establish critical time of ethanol consumption for expression of enhanced carcinogenicity of NPYR; (3) determine effect of liver damage on metabolism of NPYR, NNN. and BaP; and (4) determine effect of liver damage on carcinogenicity of NPYR.
Methods or Approach:
The effect of chronic ethanol consumption on microsomal metabolism of tobacco-associated carcinogens will be examined using specific in vitro metabolic assays. Rates of product formation will be determined and compared with controls.
Results to Date:
The influence of two methods of oral administration of ethanol to Syrian golden hamsters on microsomal metabolism and mutagenicity of NPYR and BaP have been tested. Postmitochondrial fractions (pmf) from hamsters receiving ethanol in drinking water and lab chow (low fat), showed a 50 percent decrease in ability to convert BaP to a mutagen, while this regimen did not affect ability of pmf to activate NPYR to a mutagen. In contrast, pmf from hamsters receiving ethanol in liquid diets (high fat) showed no change in ability to activate BaP to a mutagen, but exhibited an increased ability to convert NPYR to a mutagen. Hamsters receiving ethanol in drinking water and lab chow showed decreased rates of BaP metabolite formation and increased rates of α-hydroxylation of NPYR. Hamsters receiving ethanol in liquid diet form showed no change in rate of BaP metabolite formation and enhanced rates of α-hydroxylation of NPYR. Decreased microsomal BaP metabolite formation was paralleled by a decrease in specific content of microsomal cytochrome b_5. Reconstitution of purified cytochrome b_5 with microsomes isolated from ethanol-consuming hamsters caused a restoration of BaP metabolism to control levels. Results indicate the importance of the way in which oral ethanol is administered to hamsters and also suggest that cytochrome b_5 plays a role in microsomal metabolism of BaP.
Future Plans:
The minimum time for delivery of a carcinogenic dose of NPYR to hamsters will be established and the temporal relationship of carcinogen and alcohol administration will be determined.
Project Dates:
March 1981–December 1988.
Financial Support:
NCI (R01CA32126).

1348. CASE WESTERN RESERVE UNIVERSITY, SCHOOL OF DENTISTRY, Lakeside Building, Room 3570, 2074 Abington Road, Cleveland, Ohio 44106.

Project Title:
Gingival Response to Nicorette.

Principal Investigators:
Silver, K.J.; Beach, T.F.; Sachs, D.P.L., et al.
Objective:
To determine if Nicorette has any effect upon the structures of the oral cavity.
Methods or Approach:
Participants in the nonrandom, nonblind, prospective study (volunteers entering a Nicorette-based cigarette smoking cessation program) are examined prior to use of nicotine gum to determine baseline gingival condition. Clinical assessment of gingival parameters includes color, contour, consistency, and texture; periodontal (sulcus) pocket depth; bone resorption; and tooth mobility. Patients are evaluated regarding the modalities after participation in the cessation program. Gingival response is determined by comparing pre-Nicorette with post-Nicorette periodontal conditions.
Results to Date:
Use of nicotine gum showed no significant detrimental effects to oral tissue; however, in approximately 10 percent of participants, vesicular formations were found, but only on anterior hard palate tissue (maxillary) and on lingual gingiva (mandibular). Lesions were limited to 3±1 vesicle/patient. They were approximately 1 to 2 mm or less, and appearance was transient and spontaneously resolved with abstinence or changing gum use. The condition was found only in patients who held the gum in these areas for long periods of time (contrary to instructions for normal chewing). With better patient compliance, and holding in buccal mucosal area (as normally instructed) the problem ceased to exist.
Project Dates:
August 1983–June 1985.
Financial Support:
Ohio Dental Association; Merrell Dow Pharmaceutical Corp.

1349. CLEVELAND CLINIC FOUNDATION, 9500 Euclid Avenue, Cleveland, Ohio 44106.

Project Title:
Selected Psychological Characteristics of Nonsmokers, Smokers, and Ex-Smokers.

Principal Investigator:
Plesec, T.L.
Objective:
To identify characteristics that help differentiate various smoking groups (nonsmokers, smokers, and ex-smokers).
Methods or Approach:
The six groups studied will be (1) nonsmokers; (2) ex-smokers A (who have stopped smoking for at least 1 year and used a smoking cessation group program); (3) ex-smokers B (who stopped smoking by themselves and have not smoked for at least 1 year); social smokers (who smoke less than a pack/week); nonsuccessful smoking cessation group participants; and heavy smokers currently not interested in quitting (who smoke more than two packs/day). Participants will be given three psychological tests. Results will be analyzed and various smoking groups will be compared with respect to group test performances. Results could help specify characteristics important in treatment of smoking.
Results to Date:
Project is in a preliminary phase.
Project Dates:
January 1985–September 1985.

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1350. DHHS, PHS, NIH, NATIONAL INSTITUTE OF OCCUPATIONAL SAFETY AND HEALTH, R.A. Taft Laboratories, 4676 Columbia Parkway, Cincinnati, Ohio 45226.

Project Title:
Uranium Miners - Low Dose Investigation.

Principal Investigators:
Roscoe, R.; Mason, T.
Objective:
To (1) investigate cause-specific mortality patterns among uranium miners; (2) refine the dose–response curve for radon daughters and lung cancer; (3) investigate the relationship between radiation dose, cigarette smoking, latency, and histologically specific lung cancer risk; and (4) determine if an altered sex ratio of offspring of uranium miners exists.
Methods or Approach:
The investigation will include followup of a prospective cohort of 4,000 males who were underground uranium miners for at least 1 month before 1964.
Results to Date:
Followup through 1977 indicated a new excess risk of mortality due to renal disease among uranium miners. The excess risk of lung cancer, previously shown to begin after 5 years latency, now appears to be fourfold after 35 years latency, the longest followup period.
Future Plans:
Further dose- and smoking-specific analyses are planned along with followup of Indian miners, most of whom are nonsmokers.
Project Dates:
July 1975–1983.
Financial Support:
NCI; NIOSH.

1351. GROUP HEALTH ASSOCIATES, 2915 Clifton Avenue, Cincinnati, Ohio 45220.

Project Title:
Survey of Attitudes About Passive Smoking.

Principal Investigator:
Ruehlman, P.
Objective:
To (1) delineate attitudes about smoke in the workplace; (2) detail specific complaints experienced by nonsmokers, such as cough and eye irritation; and (3) survey opinions about legislation to restrict smoking.
Methods or Approach:
Employees will be surveyed.
Results to Date:
Project is in a preliminary phase.
Project Dates:
April 1985–June 1985.
Financial Support:
Group Health Associates.

1352. NORTHEASTERN OHIO UNIVERSITIES, COLLEGE OF MEDICINE, 4209 State Route 44, Rootstown, Ohio 44272.

Project Title:
Effects of Cigarette Smoke on Lung Cyclic GMP Content.

Principal Investigators:
Maron, M.B.; Braughler, J.M.
Objective:
To determine the effect of cigarette smoke, delivered through the airway, on the cyclic GMP content of a canine isolated perfused and ventilated lung preparation.
Methods or Approach:
At the beginning of an inspiration, 50 mL of the gas phase of cigarette smoke was injected into the airway of the lung preparation. After smoke exposure, periodic tissue biopsy samples were obtained for cyclic GMP content analysis (radioimmunoassay) to follow the time course of response. Additional smoke injections were made in the same lung to evaluate the repeatability of the response.
Results to Date:
Cyclic GMP content increased an average seven times by 2 seconds after smoke exposure with recovery occurring by 2 minutes after injection. Repeated smoke exposure of the same lung resulted in similar responses. Results indicate that cigarette smoke may activate lung guanylate cyclase when delivered through the airway and suggest that lung cyclic GMP levels may fluctuate acutely during smoking. Complete study results have been published.
Project Dates:
1981-July 1982.
Financial Support:
ALA; AHA; CTR.
Reference:
Maron, M.B.; Crowe, T.D.; Braughler, J.M. "Cigarette Smoke Causes Acute Fluctuations in the Cyclic GMP Content of the Isolated Intact Lung." *Respiration* 45:39-44, 1984.

1353. OHIO STATE UNIVERSITY, Department of Chemistry, Columbus, Ohio 43210.

Project Title:
Biochemical Mechanisms of Nitrosamine Carcinogenesis.

Principal Investigator:
Floss, H.G.
Objective:
To study the steric course of nucleic acid methylation by carcinogens; determine whether the stereochemical mechanism is the same (1) in vivo as in vitro; (2) for different sites on the DNA; and (3) in different tissues and species.
Methods or Approach:
The steric course of the transfer of the methyl group (made chiral by incorporating three hydrogen isotopes, H, D, and T, in an asymmetric arrangement) from four carcinogenic methylating agents, methyl methanesulfonate, methyl nitrosourea, dimethylnitrosamine (DMN), and N-methyl-N-(α-acetoxymethyl)nitrosamine, to model nucleophiles in vitro and to various sites on DNA in vitro and in vivo, will be studied. Results will indicate whether the stereochemical mechanism is the same in vivo as in vitro (suggesting that the reaction environment is similar); whether it is the same for different sites on DNA (suggesting that the nature of the nucleophile has little influence on the mechanism); and whether it is the same in different tissues and animal species (suggesting that the biological system as a whole has little influence on the mechanism). (Opposite results would lead to opposite conclusions). Results will also show whether the stereochemical fate of the methyl diazonium ion (an ultimate carcinogen) generated in three different ways in the cell is the same in each case.
Results to Date:
Methodology for studies on the steric course of DNA alkylation by chiral DMN and methylnitrosourea has been worked out, and projected work on the steric course of alkylation of simple model nucleophiles by DMN has been carried out. Work on synthesis of multiple-labeled diethylnitrosamine

(DEN) for isotope studies has been initiated. Results have been published.

Future Plans:

Future research will measure the deuterium isotope effect in metabolism of $(1\text{-}^{2}H_{1})$DEN leading to the transfer of ethyl group to DNA to determine whether all ethyl groups at different sites in DNA come from the same pool of activated species; whether DNA alkylation in different tissues of an animal draws on the same pool of activated species; and which P_{450} enzymes are most prominently involved in DEN activation in vivo. Also, the steric preference between H_R and H_S at C-1 in DEN activation in vitro and whether this preference varies for different P_{450} enzymes will be determined. Results will establish whether this parameter can also be used to characterize involvement of particular P_{450} enzymes in diethylnitrosamine activation in vivo.

Project Dates:

January 1982–December 1987.

Financial Support:

NCI (CA 37661); ACS (BC-385).

References:

(1) Floss, H.G. "Stereochemistry of One-Carbon Transfer Reactions." In: Eliel, E.L.; Otsuka, S. (Editors). *Asymmetric Reactions and Processes in Organic Chemistry.* ACS Symposium Series, No. 185, American Chemical Society, 1982, pp. 229-243. (2) Kobayashi, K.; Jadhav, P.K.; Zydowsky, I.M., et al. "A Simple and Efficient Synthesis of Chiral Acetic Acid of High Optical Purity." *Journal of Organic Chemistry* 48:3510, 1983. (3) Fatope, M.O.; Zydowsky, T.M.; Floss, H.G. "Oxidative Degradation of O^6-Methylguanine With Oxone." *Journal of Chemical Research* pp. 308-309, 1984.

1354. OHIO STATE UNIVERSITY, Department of Physiological Chemistry, 333 West 10th Avenue, Columbus, Ohio 43210.

Project Title:

Potential for Lung Cancer Prevention.

Principal Investigators:

Walaszek, A.; Webb, T.E.

Objective:

To demonstrate that susceptibility of various strains of mice to chemical carcinogen-induced pulmonary tumorigenesis is related, at least in part, to the β-glucuronidase activity and, in turn, to level of D-glucaro-1,4-lactone (GL), an endogenous β-glucuronidase inhibitor; further demonstrate that di-O-acetyl-D-glucarodilactone (DAGDL), an in vivo β-glucuronidase inhibitor, is a potent inhibitor of carcinogenesis at this site.

Methods or Approach:

It was hypothesized that susceptibility to lung tumors in various strains of mice is a function of β-glucuronidase activity, and that reducing (inhibiting) activity during exposure to carcinogens would reduce tumor induction by increasing sequestering and excretion of carcinogens as glucuronides.

Results to Date:

It has been demonstrated that DAGDL is a potent inhibitor of DMBA- and MNU-induced mammary tumorigenesis in rats (70 percent reduction in tumor incidence). It has also been proved that DAGDL suppresses up to 85 percent of carcinogen-mediated induction of 60 kd oncofetal protein (indicator of carcinogenicity) and reduces carcinogen binding to organ DNA in rats. A marked reduction (about 75 percent) was observed in DMBA binding to lung DNA in both high- and low-β-glucuronidase strains in rats. Also, inhibitory effects were observed with a wide range of carcinogens (including some tobacco-specific carcinogens) from a wide range of structural groups. Thus the approach appears to be of wide applicability.

Future Plans:

Modulation of chemical carcinogen-induced lung tumorigenesis by β-glucuronidase inhibitors will be investigated.

Project Dates:

January 1985–December 1985.

Financial Support:

CTR.

1355. UNIVERSITY HOSPITALS OF CLEVELAND, Lakeside Building, Room 3570, 2074 Abington Road, Cleveland, Ohio 44106.

Project Title:

Nicorette Dosage Study.

Principal Investigators:

Silver, K.J.; Beach, T.F.; Sachs, D.P.L.

Objective:

To predict optimal prescription dosage of Nicorette (nicotine chewing gum) for patients entering a cigarette smoking cessation program.

Methods or Approach:

Patients entering the nonrandom, nonblind, prospective study are correlated according to success in smoking cessation and nicotine gum dosage used. Prescriptions for either 2 mg or 4 mg gum are given to volunteers who desire to enter the program. Each patient is scored, using the Fagerstrom Nicotine Tolerance Test, and success or failure is compare with strength of gum used to determine if more heavily nicotine dependent patients require stronger prescriptions.

Results to Date:

Results are not yet available.

Project Dates:

August 1983–June 1985.

Financial Support:

Merrell Dow Pharmaceutical Corp.

1356. UNIVERSITY OF CINCINNATI, COLLEGE OF MEDICINE, General Clinical Research Center, University Hospital, 234 Goodman Street, Cincinnati, Ohio 45267.

Project Title:

Family Diagnosis and Therapy of Atherosclerosis Risk Factors.

Principal Investigators:

Glueck, C.J.; Morrison, J.A.; Mellies, M.J.

Objective:

To study efficacy of diagnosis, prevention, and control of major cardiovascular disease (CVD) risk factors in coronary bypass surgery patients less than 55 years of age, and in their families, in a specialized intensive program compared with customary community care.

Methods or Approach:

Probands and relatives will be randomized into three groups: in groups 1 and 2, CVD risk factors will be measured in probands and family members in a specialized clinic, while diagnosis of CVD risk factors in group 3 will be made by subjects' physicians. Abnormal risk factors in group 1 will be treated intensely over a 2-year period in a specialized clinic. Results of initial CVD risk factor measurements for group 2 families will be sent to subjects' doctors. Abnormal group 2 probands and family members will be restudied once/year, and results of their customary therapy will be compared with that of specialized therapy in group 1. In group 3, diagnosis and therapy is left to physicians; however, CVD risk factors will be measured in the specialized clinic 2 years after randomization. Risk factors in the intervention program include hyperlipidemia, obesity, and smoking. Extensive behavioral modification techniques will be used, including self-inoculation approaches to reduce smoking. Standard therapies for dyslipoproteinemia and hypertension will be used. By using two control groups, a number of important comparisons can be made. Diagnostic success will be determined by comparing the proportion of probands and family members in groups 1 and 2 vs. 3 who have CVD risk factors quantitated. Success or failure of treatment of CVD risk factors in families in a specialized facility vs. customary care therapy can be assessed and the interaction of specialized diagnosis and treatment in group 1 families can be compared with customary diagnosis and treatment in group 3 families. Motivational and environmental reasons for better indentification/therapy will be tested. Data should provide information on within-family effectiveness, safety and practicality of CVD risk factor diagnosis and therapy, intensive demonstration approaches compared with customary community care (to improve preventive medicine approaches to CVD at the community level), and how to reduce CVD morbidity and improve community cardiovascular health.

Results to Date:
Project is in a preliminary phase.

Project Dates:
December 1984–December 1987.

Financial Support:
NHLBI (1R18HL305595-0182).

1357. UNIVERSITY OF CINCINNATI, COLLEGE OF MEDICINE, 2624 Clifton Avenue, Cincinnati, Ohio 45221.

Project Title:
Effects of Nicotine on Canine Intestinal Blood Flow and Oxygen Consumption.

Principal Investigator:
Gallavan, R.H., Jr.; Tsuchiya, Y.; Jacobson, E.D.

Objective:
To determine the effects of nicotine on intestinal blood flow and oxygen consumption.

Methods or Approach:
Short-term and steady-state responses of intestinal blood flow and oxygen consumption to prolonged systemic and local administration of nicotine over a wide range of doses were examined in adult mongrel dogs.

Results to Date:
Intravenous infusion of nicotine at doses corresponding to those experienced by smokers produced a transient increase in systemic arterial blood pressure and mesenteric blood flow. Subsequently, a steady-state response developed that consisted of a reduction in mesenteric blood flow due to a decrease in blood pressure and an increase in intestinal vascular resistance (probably due to increased levels of circulating catecholamines). Intra-arterial infusion of nicotine into intestinal circulation at doses experienced by the average smoker had no effect on either intestinal blood flow or oxygen consumption. Similarly, under in vitro conditions, nicotine had no direct effect on intestinal vascular smooth muscle tension. Thus, nicotine appears to reduce intestinal blood flow indirectly as a result of systemic effects.

Financial Support:
STRC.

Reference:
Gallavan, R.H., Jr.; Tsuchiya, Y.; Jacobson, E.D. "Effects of Nicotine on Canine Intestinal Blood Flow and Oxygen Consumption." *American Journal of Physiology* 246(Gastrointestinal and Liver Physiology 9): G195-G203, 1984.

1358. UNIVERSITY OF CINCINNATI, COLLEGE OF MEDICINE, Department of Physiology and Biophysics, Cincinnati, Ohio 45267.

Project Title:
Hemodynamic Actions of Nicotine on the Canine Stomach.

Principal Investigators:
Pawlik, W.W.; Banks, R.O.; Jacobson, E.D.

Objective:
To evaluate the effects of nicotine on gastric hemodynamics and on oxygen consumption; explore effects during antagonism of α- and β-adrenergic receptors.

Methods or Approach:
Acute effects of nicotine were determined in the circulation of the stomach in which measurements of gastric blood flow, systemic arterial and portal venous blood pressures, and the arteriovenous oxygen content difference were made. From the measurements, gastric vascular resistance and oxygen consumption were calculated. Nicotine was infused for 10-minute periods in two doses intra-arterially (i.a.) and intravenously (i.v.) alone and following adrenergic receptor blockade with either propranolol or phentolamine or both.

Results to Date:
With i.a. nicotine alone, gastric blood flow and oxygen consumption increased. The effect of nicotine on blood flow was enhanced by prior treatment with phentolamine. Effects on blood flow and oxygen consumption were abolished in the presence of combined phentolamine plus propranolol. With i.v. nicotine alone, gastric blood flow, oxygen consumption, and arterial pressure increased transiently. Phentolamine enhanced the effect on oxygen uptake and prevented the pressor response. Propranolol enhanced the pressor effect, but abolished blood flow and oxygen consumption responses. Combined treatment with both adrenergic antagonists abolished nicotine effects. Findings indicate that nicotine alters gastric hemodynamics and oxygen consumption during acute intravascular infusions; effects appear to be mediated via β-adrenergic receptors. Data provide little basis for implicating a local ischemic mechanism in the ulcerogenic effects of nicotine on the stomach.

Financial Support:
STRC.

Reference:
Pawlik, W.W.; Banks, R.O.; Jacobson, E.D. "Hemodynamic Actions of Nicotine on the Canine Stomach." *Proceedings of the Society for Experimental Biology and Medicine* 177:447-454, 1984.

1359. UNIVERSITY OF CINCINNATI, COLLEGE OF MEDICINE, 3223 Eden Avenue, Cincinnati, Ohio 45267-0056.

Project Title:
Dibenzo(*c,g*)carbazole Binding to Polynucleotides and DNA.

Principal Investigator:
Lindquist, B.E.

Objective:
To (1) investigate the mechanism of action of ^{3}H-dibenzo(*c,g*)carbazole (DBC), a carcinogenic N-heterocyclic aromatic hydrocarbon that has been isolated in substantial quantities

from cigarette tar; (2) measure levels of DBC binding to various polynucleotides, DNA, and RNA in vitro; and (3) obtain information on the type of metabolites involved in this binding.

Methods or Approach:
The extent of binding is assessed by incubation of radiolabeled DBC with nucleic acid in the presence of a 3-methylcholanthrene-induced rat or hamster liver microsomal activating system. DBC binding is compared with benzo(*a*)pyrene (BaP) binding in this system to determine how this parameter relates to in vivo carcinogenicity of the two compounds. Assays are carried out in the presence of microsomal enzyme modifiers to obtain information about the metabolites involved in binding. DBC-modified nucleic acids will be digested to nucleotides and examined spectrofluorimetrically to determine which ring in the DBC molecule is involved in this binding.

Results to Date:
DBC has been shown to be metabolized to species that bind to DNA, RNA, and polynucleotides in vitro, although the extent of the binding is approximately fivefold to tenfold lower than has been demonstrated with BaP in the same experimental system. Of the various polynucleotides tested, the greatest DBC-nucleic acid binding was to polyguanylic acid, as was the case with BaP. Rat liver microsomes were more efficient than hamster liver microsomes in metabolizing DBC to nucleic acid binding species. Binding was inhibited almost completely by α-naphthoflavone, an aryl hydrocarbon hydroxylase inhibitor, but was unaffected by modifiers of epoxide hydrase activity. Evidence suggests that this binding is in the form of covalent complexes, but isolation of DBC-polyguanylic acid adducts is necessary to validate this conclusion.

Future Plans:
DBC-nucleic acid binding will be investigated in rodent tracheal organ cultures and in selected organs in the whole animal.

Project Dates:
September 1983–September 1985.

Financial Support:
NIEHS (1R01ES003409-01).

1360. UNIVERSITY OF CINCINNATI, COLLEGE OF MEDICINE, 3223 Eden Avenue, Cincinnati, Ohio 45267.

Project Title:
Chemoprotection by Dietary Indoles.

Principal Investigator:
Shertzer, H.G.

Objective:
To assess pulmonary and hepatic damage that may result from exposure to chemicals present in tobacco and tobacco smoke; study mechanism of intervention against tissue damage by chemoprotective agents such as indole-3-carbinol.

Methods or Approach:
Research is concentrating on N-nitrosamines such as N-nitrosodimethylamine and N-nitrosopyrrolidine, which require metabolic activation to express damage. Using experimental animals, isolated tissues and subcellular tissue fractions are examined for chemical damage and potential chemical intervention in such damage. Systems used assess nucleophilic and free radical components of chemical toxicity. Both enzymatic and chemical mechanisms of intervention are being examined.

Results to Date:
N-nitrosodimethylamine and related compounds exert toxicity via both nucleophilic and free radical mechanisms. Such damage is greatly ameliorated by prior treatment with indole-3-carbinol, which utilizes both mechanisms of protection. Although indole-3-carbinol may induce or inhibit monooxygenase activity, such changes do not appear to be involved in chemoprotection.

Future Plans:
Mechanisms by which dietary indole compounds protect against toxicological, mutagenic, and carcinogenic risk related to exposure to chemicals contained in tobacco and tobacco smoke will be investigated.

Project Dates:
July 1978–continuing.

Financial Support:
NIEHS (ES-03373); NCI (CA-38277).

1361. UNIVERSITY OF CINCINNATI, Department of Environmental Health, 3223 Eden Avenue, M.L. 56, Cincinnati, Ohio 45267.

Project Title:
Metabolic Activation of 7H-Dibenzo(*c,g*)carbazole.

Principal Investigator:
Strong, D.B.

Objective:
To investigate the metabolism and mechanism of action of the n-heterocyclic carcinogen, 7H-dibenzo(*c,g*)carbozole (DB(c,g)C) by (1) identification of the major metabolites of DB(c,g)C in cultures of rat hepatocytes, compared with those observed in rat liver microsomal preparations (by comparison with synthetic standards); (2) synthesis of sufficient quantities of identified metabolites for use as standards and for mutagenicity testing; and (3) determine mutagenicity of DB(c,g)C and its major metabolites in a whole-cell mutagenicity system.

Methods or Approach:
DB(c,g)C metabolites were identified and metabolites were separated by high performance liquid chromatographic techniques. Preliminary identification of metabolites was accomplished by high resolution mass spectral examination of fractions collected from microsomal incubations. Several DB(c,g)C derivatives were synthesized to aid in metabolite identity confirmation. Final identification of DB(c,g)C metabolites from microsomal and whole cell preparations was accomplished by co-chromatography with known standards. Mutagenicity of synthesized DB(c,g)C derivatives was determined in a whole cell system and mutagenesis was scored by resistance to 6-thioguanine toxicity after exposure to test compounds. Dose–response curves were generated for DB(c,g)C and benzo(*a*)pyrene (BaP) for comparison, and each derivative was individually examined at an optimum dose of 40 μm. Rates of DB(c,g)C metabolism in primary cultures of rat hepatocytes were also determined for several concentrations and compared with those found for BaP under identical conditions. Rates were determined by ^{14}C-label remaining in the aqueous layer following hexane extraction.

Results to Date:
N-heterocyclic polynuclear aromatic compounds are significant components of occupational and environmental contaminants such as coal tar, coke oven effluents, coal and oil shale processing effluents, automobile exhaust, and tobacco smoke. DB(c,g)C derivatives successfully obtained by synthetic methods were 2-, 3-, and 4-hydroxy-DB(c,g)C, n-methyl-DB(c,g)C, and 13c-hydroxy-DB(c,g)C. Attempts to obtain the n-hydroxy-DB(c,g)C derivative were not successful, but led to the n-methyl and 13c-hydroxy derivatives, which were examined for mutagenicity. Of the derivatives obtained, only 2- and 3-hydroxy-DB(c,g)C were positively identified as metabolites in both rat liver preparations, and 4-hydroxy-, n-methyl-, and

13c-hydroxy-DB(c,g)C were not found. Metabolite profiles from both preparations were qualitatively similar, but showed quantitatively different profiles. Dose–response comparisons of mutagenicity of DB(c,g)C and BaP indicated that DB(c,g)C was a significantly more potent mutagen in the whole-cell system at all concentrations tested. Of the DB(c,g)C derivatives tested, 3-hydroxy-, 13c-hydroxy-, and n-methyl-DB(c,g)C were mutagenic; 2- and4-hydroxy-DB(c,g)C were not mutagenic. Comparisons of rates of metabolism of DB(c,g)C and BaP revealed that below 25 μm in the culture medium, rates were comparable. Above 25 μm, BaP reached a plateau, while DB(c,g)C rates increased apparently linearly with dose. At 100 μm, rate of DB(c,g)C metabolism was almost four times greater than that observed for BaP. It is concluded that the nitrogen atom of DB(c,g)C is involved in the metabolic activation of the compound. Although direct oxidation of the nitrogen leading to activation cannot be ruled out, it is apparent that oxidation at other sites also leads to activated species. Thus, attack at many sites of the molecule may lead to activation. This, combined with the relatively faster rates of metabolism, helps to explain the high carcinogenicity of DB(c,g)C.

Future Plans:

Studies are being conducted to determine the activation pathways of DB(c,g)C and related n-heterocyclic polynuclear compounds, especially the dibenzacridine series.

Project Dates:

July 1983–July 1984.

Financial Support:

NIOSH (1R0301701-01); NCI (CA 23515, ES 07073).

Oklahoma

1362. OKLAHOMA STATE DEPARTMENT OF HEALTH, HEALTH EDUCATION AND INFORMATION SERVICE, P.O. Box 53551, Oklahoma City, Oklahoma 73152.

Project Title:

Occupational Stress and EMTs: Report of a State Survey.

Principal Investigators:

May, J.T.; Hann, N.E.; Richardson, R.R.

Objective:

To determine the relationship between health-related behaviors and occupational stress among emergency medical technicians (EMTs).

Methods or Approach:

Data were collected in 1984 on approximately 350 EMTs and EMT trainees, by extended interviews, field observation, and two questionnaires: (1) health hazard appraisal, and (2) demographics, occupational history, support networks, and career expectations. Analysis will focus on the relationship between health-related behaviors and occupational stress, measuring variables such as changes in smoking, alcohol use, and other health-related behaviors; conditions of employment; length of time in the profession; occupational coping skills; and support networks.

Results to Date:

Significant increases were seen in both alcohol use and cigarette smoking after EMT students were employed as licensed EMTs for at least 1 year. The most dramatic changes were in female EMTs; after working for at least 1 year, the number of smokers increased by 8 percent and the number using alcohol increased by 44.5 percent.

Future Plans:

The data base will be increased by involving EMT students and licensed EMTs from other states. Objectives will be to (1) determine level, cyclicity, and source of occupational stress; (2) identify changes in health behavior and health status related to prolonged exposure to occupational stress; and (3) develop inservice training modules for stress reduction.

Project Dates:

January 1983–continuing.

Financial Support:

Oklahoma State Department of Health.

1363. UNIVERSITY OF OKLAHOMA, HEALTH SCIENCES CENTER, P.O. Box 26901, O.U. CHB Room 305, Oklahoma City, Oklahoma 73190.

Project Title:

Risk Factors in Kidney Cancer.

Principal Investigators:

Asal, N.R.; Geyer, J.

Objective:

To investigate the role of (1) genetic factors including familial aggregation, cytogenetic determinations, and pedigree analysis (if indicated) in etiology of renal cell carcinoma; (2) occupational factors, including hydrocarbon exposure from lifetime occupational history in etiology; and (3) factors such as tobacco, beverage, alcohol, medications, history of disease, pain relievers, hormones, radiation, polymastia, and demographics. Factors will be studied individually and simultaneously by Cox's multiple linear logistic regression techniques.

Methods or Approach:

In the ongoing case–control study, 315 histologically confirmed cases of renal cell carcinoma were identified in Oklahoma hospitals between July 1, 1981 and June 31, 1984. Two controls were selected for each case: (1) 313 hospital controls (from the same hospitals where cases were identified, matched by age, sex, race, time, and hospital of admission); and (2) 336 population controls (selected by random digit techniques and frequency matching by age, sex, and race). All participants were interviewed to obtain information on major study aims.

Results to Date:

Preliminary results implicate relative weight in both men and women as a principal risk factor in renal cell carcinoma. Comparison with population controls failed to implicate cigarette smoking or beverage use as risk factors. Ever use of artificial sweeteners or sugar substitutes may be a risk factor, and ever use of beer, wine, and/or liquor is negatively associated with cancer. Work in petroleum refining and distributing increases risk and, as a group, operatives are at high risk. It is emphasized that results are preliminary and that only population controls were used.

Project Dates:

October 1981–February 1985.

Financial Support:

NCI (2R01CA31059-04).

1364. UNIVERSITY OF OKLAHOMA, HEALTH SCIENCES CENTER, Department of Social Sciences and Health Behavior, P.O. Box 26901, Oklahoma City, Oklahoma 73190.

Project Title:
Natural Reference Group School Health Education Model.

Principal Investigators:
Owens, M.; Wiist, W. Snider, G.
Objective:
To determine effectiveness of a smoking prevention program that uses peer leaders to teach friendship cliques resistance to peer pressure, decisionmaking, and self-esteem enhancement.
Methods or Approach:
Friendship cliques and peer leaders are identified among sixth grade students using a computerized algorithm sociometric analysis. In the experimental group, peer leaders will teach life skills to friendship cliques. There will be three comparison groups. In one, model students were chosen by teachers and principals to teach life skills to classmates. In the second, regular classroom teachers will instruct students in life skills. The third group will only be tested. Peer leaders and model students will receive 10 weeks of training in life skills prior to participating in the 10-week program. A questionnaire was administered to 332 students to assess knowledge of decisionmaking skills, methods of resisting peer pressure, self-concept, and use of tobacco. All students will be posttested to assess changes in life skills and tobacco use.
Results to Date:
Project is in a preliminary phase.
Future Plans:
Effectiveness of the program in reducing alcohol and drug abuse will also be analyzed. The second phase of the project will use friendship groups and peer leader instruction in health promotion subjects such as nutrition, exercise, and stress reduction.
Project Dates:
October 1984–October 1986.
Financial Support:
ALA.

1365. UNIVERSITY OF OKLAHOMA, Department of Chemistry, Norman, Oklahoma 73019.

Project Title:
Diol Epoxide and Other Derivatives of PAH and Aza-PAH: Structure-Activity Relationships.

Principal Investigator:
Lehr, R.E.
Objective:
To determine structure–activity relationships that influence relative carcinogenicity of polycyclic aromatic hydrocarbons (PAHs); determine mechanism by which PAHs induce cancer.
Methods or Approach:
Diol epoxide, dihydrodiol, and other derivatives of PAHs are synthesized and tested for mutagenicity and carcinogenicity through collaborations. Attempts are made to determine (through calculations and measurement) any relationships between biological activity and chemical reactivity.
Results to Date:
A number of factors influencing biological activity of diol epoxide derivatives of PAHs and aza-PAHs have been identified (through this research and through that of other researchers), including (1) electronic factors, especially the stability of the carbocation resulting from heterolytic cleavage of the benzylic C-O bond of the epoxide; (2) conformational factors, with diol epoxides that have pseudodiaxial hydroxyl groups having diminished activity; (3) steric factors, with epoxides that occupy a highly hindered region being apparently especially biologically active; and (4) topological factors, with only diol epoxides with the epoxide in a bay region position being found to be tumorigenic (to date).
Future Plans:
Additional PAH derivatives will be synthesized and studied, with emphasis on sterically hindered diol epoxides and tetrahydroepoxide.
Project Dates:
December 1982.
Financial Support:
NCI (CA 22985).

Oregon

1366. AMERICAN HEART ASSOCIATION, OREGON AFFILIATE, Task Force on Smoking and Health, 1500 SW. 12th Avenue, Portland, Oregon 97201.

Project Title:
The Role of the Oregon Primary Care Provider in Smoking Cessation.

Principal Investigators:
Conrad, E.E., Jr.; Sanders, L.
Objective:
To determine and optimize methods used by Oregon health care professionals to foster smoking cessation in patients.
Methods or Approach:
Health care professionals in Oregon (physicians, nurses, chiropractic physicians, dentists) will be surveyed by direct mail regarding practices used in fostering smoking cessation in patients. This will be followed by a series of information mailings and, ultimately, by a second survey.
Results to Date:
Project is in a preliminary phase.
Project Dates:
June 1984–June 1986.
Financial Support:
AHA.

1367. KAISER PERMANENTE CENTER FOR HEALTH RESEARCH, 4610 SE. Belmont, Portland, Oregon 97215.

Project Title:
Preventing Drug Abuse Relapse - Smoking as a Prototype.

Principal Investigators:
Stevens, V.J.; Hollis, J.
Objective:
To determine effectiveness of a coping skills training approach to prevention of relapse in ex-smokers; test usefulness of a pretreatment questionnaire in predicting situations that are likely to lead to relapse in an ex-smoker.
Methods or Approach:
Adult smokers are provided help in quitting in a 4-day, intense

cessation program. Those who quit are randomly assigned to (1) no treatment control group, (2) coping skills training and rehearsal group, or (3) social support control group. Measurements of outcome will be biochemically confirmed at 12-months posttreatment.

Results to Date:

Intervention was completed for 746 subjects in 1984; 77.4 percent were randomized into one of the followup treatment conditions.

Future Plans:

Final assessment of smoking status will be made in 1985 (end of 12-month followup).

Project Dates:

January 1984–December 1985.

Financial Support:

NIDA (1R01DA03538-01).

1368. LEWIS AND CLARK COLLEGE, Department of Psychology, Portland, Oregon 97219. CENTER FOR HEALTH RESEARCH, KAISER-PERMANTE MEDICAL CARE PROGRAM, 4610 SE. Belmont, Portland, Oregon 97215.

Project Title:

Attributions for Abstinence, Nonabstinence, Lapse and Relapse Following Smoking Cessation Treatment.

Principal Investigators:

Schoeneman, T.J.; Cheek, P.R.; Kischer, K., et al.

Objective:

To (1) compare types of causal attributions for lapses (slips) made by ex-smokers who return to abstinence vs. those who relapse; (2) compare types of causal attributions for current nonsmoking or smoking status made by four posttreatment groups (totally abstinent, never abstinent, initially abstinent but relapsed, and initially abstinent with lapse and return to abstinence); and (3) assess relationship between causal attributions made and perceived likelihood of smoking in the future.

Methods or Approach:

Eighty people from the Portland, Oregon, metropolitan area completed the Kaiser-Permanente Freedom From Cigarettes program. One to two years after treatment, they were contacted by telephone and asked to complete a 15- to 30-minute interview, which included questions about current smoking status, circumstances of posttreatment lapse (if any), attributions and emotions for initial lapse (if any), attributions and emotions for current smoking or nonsmoking status, and perceived likelihood of smoking in 3 months.

Results to Date:

To date, 68 of the 80 participants (85 percent) have been contacted: 22 are abstinent (with no lapses), 15 never abstinent, 7 lapsed but currently abstinent (slip-abstinent), and 17 relapsed (slip-relapse); 7 refused to participate. Slip-abstinent subjects explained slips as due to personally changeable factors, whereas slip-relapse subjects saw initial slips as less changeable. In explaining causes of current smoking or nonsmoking status, subjects in all groups tended to make internal attributions; abstinent and slip-abstinent subjects emphasized causes that were more personally controllable, more stable over time, and more general across situations than did never abstinent and slip-relapse subjects.

Future Plans:

Interviews will be completed and analyses will relate outcomes, attributions, emotions, likelihood estimates, and a pretreatment scale of self-efficacy for smoking abstinence.

Project Dates:

June 1982–June 1985.

Financial Support:

Lewis and Clark College; Center for Health Research.

1369. OREGON HEALTH SCIENCES UNIVERSITY, 3181 SW. Sam Jackson Park Road, Portland, Oregon 97201.

Project Title:

Self-Generated Smoking Cessation and Reasons for Never Smoking.

Principal Investigators:

Pierce, D.K.; Brischetto, C.S.; Carmody, T., et al.

Objective:

To (1) examine quitting patterns and reasons for quitting in a sample of ex-smokers; (2) determine reasons why nonsmokers never started; and (3) follow up ex-smokers to evaluate how well cessation is maintained over a period of 5 years.

Methods or Approach:

Subjects are 120 ex-smokers who are part of the Family Heart Study, an ongoing intervention project aimed at dietary change to reduce risk for heart disease. There is increasing interest in how millions of Americans stop smoking without the help of professionals, and ex-smokers in this population quit on their own. A specially designed questionnaire is used to examine reasons for quitting, how subjects quit, and any consequences of quitting. Information on long-term followup is also recorded. Questions related to reasons for not smoking were given to nonsmokers. Questionnaires were administered in the form of structured interviews conducted by a team of medical psychologists in the Family Heart Study.

Results to Date:

Results are not yet available.

Project Dates:

January 1984–January 1986.

Financial Support:

NHLBI (5R01HL20910-08).

1370. OREGON HEALTH SCIENCES UNIVERSITY, 3181 SW. Sam Jackson Park Road, Portland, Oregon 97201.

Project Title:

Natural History of Chronic Airflow Obstruction.

Principal Investigator:

Buist, A.S.

Objective:

To (1) determine the predictive value of the single breath N2 test in identifying the individual who is going to progress to chronic airfow obstruction; (2) determine the contribution of various host and environmental factors to development of chronic airflow obstruction; and (3) obtain further information about how lungs age and what factors affect aging.

Methods or Approach:

Data was collected on (1) respiratory symptoms, smoking habits, chest illnesses, occupation, residence, and family history of chest problems (obtained by questionnaire); (2) pulmonary function tests (spirometric tests before and after a bronchodilator and single breath N2 test, a test of small airway function); (3) trypsin inhibitory capacity and phenotyping for α_1-antitrypsin deficiency; (4) serum immunoglobulin E; (5) skin tests to five common allergies; and (6) response to an aerosolized inhaled bronchodilator as an index of airway reactivity. Subjects were tested either annually or biennially. Total followup time varied between 10 and 12 years.

Results to Date:

Data analysis indicates that both the single breath N2 test and response to an inhaled bronchodilator are useful in identifying the individual with a more rapid than expected decline in forced expiratory volume in 1 sec. Analysis of data is continuing.

Project Dates:
December 1979–May 1985.

Financial Support:
NHLBI (R01HL24918-06).

1371. OREGON RESEARCH INSTITUTE, 195 West 12th Avenue, Eugene, Oregon 97401.

Project Title:
Evaluation of a Worksite Smoking Control Program.

Principal Investigators:
Glasgow, R.E.; Klesges, R.C.

Objective:
To (1) investigate incremental effects on participation rate and treatment outcome of adding social support and competition procedures to a standardized worksite smoking control program; (2) compare relative effectiveness of a smoking control program offering the option of controlled smoking to a multicomponent abstinence-based cessation program; and (3) identify employee and organizational characteristics and treatment process variables associated with treatment outcome.

Methods or Approach:
A series of comparative outcome studies is being conducted in a number of different worksite settings to investigate the incremental effects of adding various components to a basic smoking control program. Participants meet in small groups (four to eight persons) for six weekly sessions. Program components include self-monitoring, nicotine fading, number reduction, and relapse prevention training. Dependent variables include validated questionnaire measures of smoking patterns, carbon monoxide, and thiocyanate.

Results to Date:
Neither coworker nor significant other social support procedures appear to improve the effectiveness of the basic smoking control program. Competition betweeen worksites apparently increases the percentage of participants, but the effect on treatment outcome is less clear. Nonabstinent subjects who completed the program were able to maintain reductions in smoking behavior (including carbon monoxide changes) at followup after 2.5 years.

Future Plans:
Computer-assisted and self-help versions of the program will be developed that can be utilized in the worksite and the relative effectiveness of these approaches vs. the more traditional group therapy approach will be evaluated.

Project Dates:
August 1983–July 1986.

Financial Support:
NHLBI (HL 33739).

1372. OREGON RESEARCH INSTITUTE, 195 West 12th Avenue, Eugene, Oregon 97401.

Project Title:
Family Influence on Adolescent Smoking.

Principal Investigators:
Hops, H.; Sherman, L.; Lichtenstein, E.

Objective:
To (1) determine the extent of parent and sibling influence on adolescent smoking decisions; (2) evaluate the relative strength of these sources of influence compared with peer influence; (3) elucidate specific mechanisms or psychological processes by which families influence children's smoking decisions; (4) obtain observational data on smoking-related family interactions; and (5) compare findings with questionnaire and interview data.

Methods or Approach:
Nine hundred families will serve as subjects; a subset of 150 will receive more intensive assessment. Four estimates of parental and sibling influence on adolescent smoking and drug usage will be obtained: (1) from parent and adolescent questionnaire; (2) by examining discrepancies between parent and adolescent reports on comparable variables; (3) from observational data on problem-solving interactions about smoking and other drug-related issues; and (4) from parent and adolescent interviews. Subjects will be followed up for 2 years. Data will allow both cross-sectional and prospective analyses using structural equation modeling and multivariate analysis of variance methods.

Results to Date:
Project is in a preliminary phase.

Project Dates:
July 1984–June 1988.

Financial Support:
NIDA (1R01DA03706).

1373. OREGON RESEARCH INSTITUTE, 195 West 12th Avenue, Eugene, Oregon 97401.

Project Title:
Adolescent Chewing Tobacco Use and Smoking Prevention.

Principal Investigator:
Severson, H.H.

Objective:
To (1) evaluate the role of chewing tobacco in development of adolescent smoking; (2) determine effects of deprivation of one tobacco product on topography/rate of both products; and (3) assess previous progress with antichewing component.

Methods or Approach:
Research will (1) combine an experimental evaluation of smoking prevention programs with an in-depth longitudinal study of development of both smokeless tobacco use and cigarette smoking, and (2) experimentally analyze potential of smokeless tobacco to promote cigarette smoking. The prevention program (seventh and ninth grade students) will compare two curricula: smoking prevention only and tobacco chewing prevention plus smoking prevention. Treatments are compared with each other and with a control group to assess whether addition of antichewing materials increases effectiveness of prevention program by deterring smoking. Students in grades 6 through 11 will be studied to identify cross-sectional and longitudinal predictors of smokeless tobacco use and smoking. Questionnaires and physiological measures are used to evaluate the full sample of 4,000 students over a 3-year period. A subsample of 384 students from control and treatment conditions is studied in depth using interviews, telephone probes, parent interviews, and parent-child interaction tasks. For subjects who use both substances, studies will examine effects of deprivation of one substance on topography and rate of consumption of the other substance. Effects of deprivation on subject's craving in their natural environment will also be studied. Analysis will determine effects of using chewing tobacco on probability of subsequently becoming a smoker.

Results to Date:
Pretest assessment of 6th through 11th grade students in 11 middle and high schools is underway. Intervention will take place in January and February 1985. Results are not yet available.

Project Dates:
May 1984–April 1988.
Financial Support:
NIDA (1R01DA03635-01).

1374. PORTLAND STATE UNIVERSITY, Health Education Division, Box 751, Portland, Oregon 97207.

Project Title:
Smoking and Health Education Experiments, Demonstrations, and Exhibits.

Principal Investigator:
Gilbert, G.G.
Objective:
To (1) revise the publication "Smoking and Health Experiments, Demonstrations and Exhibits"; (2) review educational literature of appropriate classroom experiments and demonstrations; and (3) pilot test materials for inclusion and publication in the revised document.
Methods or Approach:
The literature will be reviewed and useful examples will be selected teacher's guide for the revised publication will be prepared.
Results to Date:
Additional experiments and demonstrations have been located to update the publication.
Project Dates:
November 1984–December 1985.
Financial Support:
OSH.

1375. UNIVERSITY OF OREGON, SCHOOL OF MEDICINE, Health Sciences Center, Division of Environmental Medicine, 3181 SW. Sam Jackson Park Road, Portland, Oregon 97201.

Project Title:
Epidemiology of Lung Cancer in Oregon.

Principal Investigator:
Morton, W.E.
Objective:
To (1) identify spatiotemporal patterns of mortality throughout Oregon since 1953; (2) search for high-risk areas of residence and high-risk occupations in both sexes; (3) identify spatiotemporal patterns of histology-specific incidence in the Portland–Vancouver metropolitan area since 1963; and (4) determine high-risk areas of residence and high-risk occupations.
Methods or Approach:
The following data have been collected: (1) sex-specific, age-standardized, mean annual death rates for 5-year periods since 1953 for all counties; (2) occupations from death certificate copies since 1963; (3) all cases occurring in the Portland metropolitan area during 1963-1977 by search of tumor registries and hospital record rooms; and (4) age-adjusted incidence rates by sex for geographic regions, socioeconomic strata, and occupation categories.
Results to Date:
Rising lung cancer mortality rates during 1953-1982 were similar for both sexes in all parts of Oregon; the steepest increases were among women living in the coastal counties. Preliminary incidence data (1968-1972) in the Portland metropolitan area showed that the different histologic types had different socioeconomic, geographic, and occupational high-risk patterns, suggesting that they should be regarded as different diseases. Major sex differences in socioeconomic patterns of risk suggested the importance of occupational confounding among men. Occupational risk differences among both sexes far exceeded those noted with other risk factors, suggesting that occupational exposures deserve primary emphasis in future efforts at lung cancer control.
Future Plans:
Causes of lung cancer other than smoking which are associated with particular occupations will be identified in the hope of eventually reversing the epidemic trend of this disease.
Project Dates:
June 1974–continuing.

1376. UNIVERSITY OF OREGON, Department of Psychology, Eugene, Oregon 97403.

Project Title:
Cluster Analysis of Relapse Episodes and the Prediction of the Nature of Relapse.

Principal Investigators:
Baer, J.S.; Lichtenstein, E.
Objective:
To empirically characterize the nature of relapse episodes using cluster analysis techniques; prospectively predict in what kinds of situations subjects are likely to relapse, utilizing individual difference information.
Methods or Approach:
Telephone interviews probing the nature of relapse episodes are used to provide descriptive information about such episodes. Cluster analytic techniques are applied to the data. Smoking history and other psychosocial data obtained from participants are then related to the relapse episodes.
Results to Date:
Results are not yet available.
Project Dates:
June 1984–December 1985.
Financial Support:
University of Oregon.

1377. UNIVERSITY OF OREGON, Department of Psychology, Eugene, Oregon 97403.

Project Title:
Program Adherence and Coping Strategies in Smoking Cessation and Maintenance.

Principal Investigators:
Kararck, T.W.; Lichtenstein, E.
Objective:
To (1) identify quitting strategies used by subjects in a social learning-based smoking cessation program; (2) determine predictors of strategy use and relationship between strategy use and treatment outcome and maintenance; and (3) examine use of various strategies after treatment and the relationship with maintenance of nonsmoking.
Methods or Approach:
Measures of program adherence and coping strategies, in treatment and after treatment, were developed and obtained from approximately 100 subjects. Measures will be related to smoking outcomes up to 6 months posttreatment. Causal modeling procedures will be used to test hypotheses about coping predictors, program adherence, and treatment outcome.
Results to Date:
Results are not yet available.
Project Dates:
May 1984–December 1985.
Financial Support:
University of Oregon.

1378. UNIVERSITY OF OREGON, Department of Psychology, Eugene, Oregon 97403.

Project Title:
Psychosocial Stress, Social Support and Smoking Cessation.

Principal Investigators:
Lichtenstein, E.; Cohen, S.; Mermelstein, R.J.

Objective:
To test hypotheses about the effects of social support, psychosocial stress, and their interaction on smoking cessation and maintenance.

Methods or Approach:
Subjects, all participants in smoking cessation programs, met in small groups for six weekly sessions. Smoking status was assessed periodically for 1 year posttreatment, and self-reports were corroborated by significant other reports and physiological measures. Participants were given measures of stressful life events, perceived stress, partner support for quitting smoking, and general social support. Data were analyzed to determine influence of psychosocial stress and social support on cessation and maintenance. Of particular interest will be a test of the "buffering" hypothesis that social support can mitigate effects of life stress.

Results to Date:
Support specific to quitting smoking and more general perceived social support were related to successful smoking cessation. Perceived stress experienced after treatment was predictive of smoking reduction at followup. Evidence of a buffer effect (an interaction for stress and social support) was found for posttreatment cessation but not for maintenance.

Future Plans:
The stress and social support framework will be extended to the study of unaided smoking cessation.

Project Dates:
August 1982–April 1985.

Financial Support:
NHLBI (HL 29547)

1379. UNIVERSITY OF OREGON, Department of Psychology, Eugene, Oregon 97403.

Project Title:
Partner Support and Smoking Cessation.

Principal Investigators:
Lichtenstein, E.; Mermelstein, R.J.; McIntyre, K.O.

Objective:
To develop and evaluate a partner support program to enhance the effectiveness of a social-learning-based smoking cessation program.

Methods or Approach:
Two intervention studies were conducted in which a social-learning-based skills training program only was compared with the skills program plus a social support component. Participation of a spouse or partner in the treatment program constituted the social support component. All subjects met in small groups for six weekly sessions. Followup smoking status was assessed periodically through 1 year posttreatment, and self-reports were corroborated by significant other reports and physiological measures. Participants were also given measures of partner support for quitting smoking (via the Partner Interaction Questionnaire) and general social support.

Results to Date:
Subjects who were successful abstainers 6 months posttreatment had higher social support than subjects who never quit or those who quit and relapsed. While partner support condition tended to have more successful outcomes, differences between conditions were not statistically significant at any assessment.

Project Dates:
January 1982–April 1985.

Financial Support:
NHLBI (HL 29547).

1380. UNIVERSITY OF OREGON, Department of Psychology, Eugene, Oregon 97403.

Project Title:
The Role of Self-Efficacy in the Maintenance of Smoking Cessation.

Principal Investigators:
Lichenstein, E.; Baer, J.S.; Holt, C.

Objective:
To evaluate the predictive and construct validity of self-efficacy as a mediator of maintenance of smoking cessation; identify some of the antecedents of efficacy.

Methods or Approach:
A measure of subjects' self-efficacy (confidence that they could refrain from smoking in a variety of situations) was administered at the end of a social-learning-based smoking cessation program. Subjects were followed up periodically for a year, and self-efficacy probes were administered up to 6 months posttreatment. Data from three separate studies have been analyzed (approximately 170 subjects).

Results to Date:
Posttreatment efficacy ratings are consistently and strongly correlated with smoking status and smoking rate at followup; however, smoking rates during the final week of treatment are an even stronger predictor. When smoking rate at end of treatment is partialled out, small but significant correlations between efficacy ratings and posttreatment maintenance remain. Few antecedents of posttreatment efficacy could be identified; amount of smoking by subjects after target quit date is the major antecedent predictor. Contrary to theoretical expectation, self-efficacy does not appear to mediate effects of other predictor variables on smoking outcomes. Confidence ratings made during followup are highly related to subsequent smoking status.

Project Dates:
January 1982–April 1985.

Financial Support:
NHLBI (HL 29547).

1381. VETERANS ADMINISTRATION MEDICAL CENTER, P.O. Box 1034, Portland, Oregon 97297.

Project Title:
Spirometric "Lung Age" Estimation for Motivating Smoking Cessation.

Principal Investigators:
Morris, J.F.; Temple, W.

Objective:
To calculate the functional age of a person from pulmonary function testing (spirometry) that can be used as a psychological tool to motivate smoking cessation.

Methods or Approach:
Equations are derived from reference linear regression equations for healthy nonsmoking adults previously obtained by this laboratory from an Oregon population. The new equations permit estimation of functional lung age. Comparison with the person's chronological age indicates the degree of premature aging and impairment from inhaling tobacco smoke.

Results to Date:
The relative validity of the different components of the forced vital capacity (FVC) maneuver was determined by obtaining the standard error (SE) for each component. The SE represented the standard deviation of the differences between chronological and estimated lung age for each test of 988 normal subjects. The best result was for the forced expiratory volume in 1 sec (FEV$_1$), which had the lowest SE. Similarly, the FEV$_1$ lung age best discriminated between one group of 22 normal subjects and 37 patients with chronic obstructive pulmonary disease due to smoking. In an urban emphysema screening center, spirometry and lung estimation resulted in a smoking cessation rate of 20 percent after 3 years.

Future Plans:
Application of lung estimation will be incorporated into smoking cessation projects using spirometry as an educational tool for smoking cessation.

Project Dates:
June 1983–July 1986.

Financial Support:
VA; Oregon Lung Association.

Pennsylvania

1382. ALLEGHENY COUNTY HEALTH DEPARTMENT, 3333 Forbes Avenue, Pittsburgh, Pennsylvania 15213.

Project Title:
Allegheny County Health Department Employee Smoking Survey.

Principal Investigators:
Synkewecz, C.A.; Hennon, D.; Donfield, S.

Objective:
To (1) enable employees to share information relating to smoking habits, policy opinions, and educational needs; (2) understand the extent of smoking by employees; (3) identify resolutions to conflicts; (4) review acceptance of current policy and revise if necessary; and (5) gain insight into problem areas for policy implementation.

Methods or Approach:
A questionnaire was developed and distributed to all employees in the summer of 1984; 417 persons (63 percent) participated. A data-based management system was used for analysis.

Results to Date:
Among respondents, 26 percent reported smoking; the largest number were in the clerical/technical job category. Prevalence of smoking by occupation was administrators, 17.4 percent; clerical/technical, 32.7 percent; supervisors, 35.4 percent; professional, 17.6 percent; other, 31.6 percent. In terms of current policy satisfaction, 56 percent of those who knew the policy reported satisfaction with it. It is important to note that over 50 percent expressed some irritation in the presence of smoke. Approximately 57 percent of smokers stated the desire to reduce consumption, and 70 percent were willing to participate in a smoking cessation program sponsored by the health department. Policy suggestions included smoking restricted to specific areas (53 percent) and restricting smoking where complaints exist (20.9 percent). The least popular suggestions were to allow unrestricted smoking (8.6 percent) and to prohibit smoking (16.3 percent).

Future Plans:
A new Employee Smoking Policy was drafted and will be approved and implemented in 1985. A smoking cessation program will also be implemented for interested employees.

Project Dates:
May 1984–September 1984.

Financial Support:
Allegheny County Health Department.

1383. ALLEGHENY COUNTY HEALTH DEPARTMENT, BUREAU OF HEALTH EDUCATION, 40th and Pennsylvania Avenue, Pittsburgh, Pennsylvania 15224.

Project Title:
Survey of Curriculum and Materials: Smoking Education in Allegheny County Elementary and Secondary Schools.

Principal Investigators:
Meenihan, R.J.; Donfield, S.; Kerr, D.

Objective:
To (1) determine the content of and materials used for smoking education in elementary and secondary schools in Allegheny County (Pittsburgh); (2) assess depth of smoking education programs; and (3) provide suggestions to educators, administrators, and program planners within the Health Education division.

Methods or Approach:
Specifically, the project will determine (1) whether smoking education is included in a school's health curriculum; (2) what smoking-related topics are examined; (3) how content varies by grade level and school; (4) the discipline responsible for providing smoking education; (5) person or organization responsible for maintaining smoking education materials; and (6) smoking policies of schools. In the first phase, a two-page survey was mailed to principals of the 557 public and private elementary and secondary schools in the county. In the second phase, a random sample of 1,000 teachers will be selected from listings supplied by districts. The secondary school sample will be limited to instructors of health and physical education, general science, biology, sociology, and psychology. A survey form (identical to that used in the first phase) will be mailed to selected teachers. Following data collection, all information will be entered into a computer and descriptive and analytic statistics will be generated. Of particular interest will be program comparisons by grade level, geographic area, and public vs. private school curriculum.

Results to Date:
To date, 404 principals (72.5 percent) have responded and followup is in progress. Sampling frames for the teachers' survey are being finalized. Teacher listings have been supplied by 43 of the 44 school districts.

Project Dates:
June 1984–March 1985.

Financial Support:
Allegheny County Health Department.

1384. BEAVER COLLEGE, Glenside, Pennsylvania 19038.

Project Title:
The Relation of Pattern of Support for Smoking and Achievement Motive in Young Women.

Principal Investigators:
Mausner, B.; Brandspiegel, D.
Objective:
To test the hypothesis that the supports for smoking are not uniform among young women and that those who are high in achievement orientation tend to smoke to release tension caused by striving, especially when they are engaged in nontraditional occupations.
Methods or Approach:
Because smoking is increasing among young women in contrast to decreases in the rest of the population, it is vital to understand the role that smoking plays in their lives. Smoking may be used to support a self-concept as an emancipated person. In contrast, it is hypothesized that smoking among women low in achievement orientation will be supported by social or hedonic factors. Thirty female students at a small liberal arts college, randomly selected from dormitory students who smoke regularly, were given the Mehrabian Test for need achievement and a measure of sources of support for smoking developed by Mausner and Platt. Subjects were divided into groups above and below the median for need for achievement. Mehrabian scores were correlated with scores on the various supports for smoking, and support scores were compared.
Results to Date:
As predicted, analysis showed four significant correlations with subscales on the measure of patterns of support (out of eight possible relationships). Subjects high in need to achieve were significantly more likely to report smoking for tension release and to support self-concept than those low in need to achieve. Significant correlations were found for psychological addiction, habit/self-image, social/self-image, and tension release. It is concluded that young women oriented toward achievement smoke to reduce tension and to support self-image, and as part of a habitual pattern. Those not so oriented smoke for other reasons.
Future Plans:
The ecologic pattern of smoking will be studied by use of diaries.
Project Dates:
September 1982–June 1983.

1385. CARNEGIE-MELLON UNIVERSITY, Department of Psychology, 5115 Margaret Morrison Street, Pittsburgh, Pennsylvania 15213.

Project Title:
Stress and Social Support in the Self-Quitting of Smoking (Human).

Principal Investigator:
Cohen, S.
Objective:
To elucidate the psychosocial factors critical to maintenance or relapse in self-quitting of smoking and to evaluate the outcomes of prototypical ways in which smokers try to quit without the help of formal programs.
Methods or Approach:
Psychosocial factors to be examined include stressful life events, perceived stress, social support, social network characteristics (interactions with other smokers), and coping strategies. Covariation and interaction of factors with relapse or maintenance will be compared in four groups of subjects: New Year's resolution quitters, participants in two instruction manual programs, and an instruction manual plus four optional group sessions program. Results will also be compared with previous work on clinic-aided quitting. Smoking status and information on psychosocial factors will be obtained by telephone interview 1, 2, 3, 6, and 12 months after the initial attempt at cessation. Multivariate procedures will be used to evaluate the relation of psychosocial factors to outcome. Reactivity of the assessment procedures will be experimentally evaluated by comparing groups that receive minimal assessment with those receiving the entire assessment battery. Outcomes and cost effectiveness of the four programs will be determined. It is anticipated that the programs providing more assistance (group sessions) will be more successful but less cost-effective than programs providing minimal assistance.
Results to Date:
Project is in a preliminary phase.
Project Dates:
August 1984–July 1988.
Financial Support:
NCI (1RO1CA38243-01).

1386. FOX CHASE CANCER CENTER, 7701 Burholme Avenue, Philadelphia, Pennsylvania 19111.

Project Title:
A Survey of Physicians' Views and Practices About Patient Education for Smoking Cessation.

Principal Investigators:
Rimer, B.K.; Keintz, M.K.; Strecher, V.J., et al.
Objective:
To determine (1) what types of smoking cessation strategies physicians used prior to the availability of nicotine chewing gum; (2) how strategies varied by physician's specialty, personal smoking status, and beliefs in efficacy and health outcomes of smoking cessation efforts; (3) how the intention to use nicotine gum correlate with actual use following market availability; (4) how intentions to prescribe gum influenced physicians; and (5) to develop cost-effective smoking cessation programs that physicians can use with patients.
Methods or Approach:
A random sample of physicians received questionnaires concurrent with the introduction of nicotine chewing gum in the United States. A second questionnaire was mailed 6 months later. A second group of physicians received only the second questionnaire, to permit examination of the effects of pretesting on subsequent results.
Results to Date:
The most frequently used health education strategies were recommendations and counseling. Family practitioners used more strategies, including written information and referral in addition to counseling. Of the physicians responding, 87 percent were aware of Nicorette (nicotine chewing gum). Initial response showed that 68 percent intended to prescribe the gum, and 90 percent of those actually did prescribe use of the gum. Along with prescribing the gum, 23 percent intended to increase health education efforts. Over 60 percent reported an interest in attending a continuing medical education course on smoking cessation.
Future Plans:
Continuing medical education courses and smoking cessation interventions that can be used with patients will be developed.
Project Dates:
March 1984–continuing.
Financial Support:
Fox Chase Cancer Center.

1387. FOX CHASE CANCER CENTER, 7701 Burholme Avenue, Philadelphia, Pennsylvania 19111.

Project Title:
Cancer Control in an Urban Neighborhood.

Principal Investigator:
Amsel, Z.

Objective:
To (1) assess the feasibility of a prototypic community-based cancer control program designed to reduce the incidence and mortality due to cancer in an urban neighborhood identified as a high risk area (through analysis of mortality data); (2) identify community residents at high risk; and (3) reduce the risk by screening and health education interventions.

Methods or Approach:
The epidemiological and psychological effectiveness of the program will be measured by (1) comparing the intervention community with a comparison community matched for ranking of cancer mortality, racial and age composition, and industrial concentration; and (2) assessing the effectiveness of each program component in achieving its intended effects.

Results to Date:
During the first 15 months of the project, a baseline community survey was conducted in the intervention and comparison areas, collecting information on knowledge, attitudes, experiences, and practices related to cancer and heart disease. A mail approach elicited a 23 percent (1,538) and 30 percent (1,122) response from the intervention and comparison areas, respectively. Data are being used to develop health education programs. Project staff have developed strong working relationships with leaders of community groups through public awareness campaigns, which will be ongoing throughout the project. The staff also worked with a local community hospital to design a multisite screening and detection unit that incorporates health education, counseling, and referrals.

Future Plans:
Self-administered risk assessment forms will be distributed to identify individuals at risk so recommendations can be made on ways to reduce risk, and a smoking cessation support program will be developed, geared specifically for this blue-collar area. A cancer education and counseling program will be introduced in industries.

Project Dates:
July 1983–June 1988.

Financial Support:
NCI (CA 34856).

1388. HAHNEMANN MEDICAL COLLEGE AND HOSPITAL, 3912 Netherfield Road, Philadelphia, Pennsylvania 19129.

Project Title:
Lung Cancer Due to Chloromethyl Ethers.

Principal Investigator:
Weiss, W.

Objective:
To determine (1) the risk of lung cancer in a cohort of chemical workers exposed to chloromethyl ethers during the period from 1948 to 1971; (2) the cancer type involved; (3) the dose-response relationship; and (4) the influence of smoking.

Methods or Approach:
A cohort of 125 workers (91 exposed to chloromethyl ethers) has been followed since 1963 and semiquantitative estimates of degree of exposure and records of duration of exposure have been maintained. Information on smoking habits was obtained at the beginning of the observation period. The incidence of lung cancer is determined periodically.

Results to Date:
Over the 22 years of followup, exposed workers have had a very high risk of respiratory cancer, mostly of the lung. The risk has been dose-related and has been much higher in nonsmokers and ex-smokers than in current smokers. The epidemic began to subside shortly after exposure to chloromethyl ethers ceased. The mean induction–latency period was 17 years. Most of the lung cancers in the moderate and high dose groups have been small cell carcinomas.

Future Plans:
The cohort will be followed up indefinitely.

Project Dates:
December 1962–continuing.

1389. HAHNEMANN MEDICAL COLLEGE AND HOSPITAL, 3912 Netherfield Road, Philadelphia, Pennsylvania 19129.

Project Title:
Smoking and Asbestos-Related Pleural Plaques.

Principal Investigator:
Weiss, W.

Objective:
To determine the incidence of asbestos-related pleural plaques in smokers, nonsmokers, and ex-smokers.

Methods or Approach:
A group of workers exposed to asbestos has been followed up with periodic chest x rays for a period of years. Smoking habits have been recorded. The first and last postero-anterior chest films will be evaluated for the development of pleural plaques in relation to smoking habits.

Results to Date:
Results are not yet available.

Project Dates:
December 1984–December 1986.

1390. HAHNEMANN UNIVERSITY, SCHOOL OF MEDICINE, Room 421, Bellet Building, 1505 Race Street, Philadelphia, Pennsylvania 19102.

Project Title:
Temporal Relationship Between Cigarette Smoking and Pancreatic Cancer in the U.S.

Principal Investigator:
Weiss, W.

Objective:
To study the relationship between the percentage of adult smokers from 1920 to 1978, and the age-adjusted pancreatic cancer mortality rate from 1935 to 1978, by sex.

Methods or Approach:
Estimates of U.S. cigarette smoking prevalence rates by sex, published for 1920-1965 by Burbank and 1970-1978 by Moss, have been graphed with U.S. age-adjusted pancreatic cancer mortality rates by race and sex as reported by Devesa and Silverman. Additional rates for 1978 were calculated from data supplied by the National Center for Health Statistics and the Bureau of the Census.

Results to Date:
Temporal trends in U.S. cigarette smoking prevalence rates for 1920 to 1978 were related to temporal trends in U.S. pancreatic cancer mortality rates in both sexes. In males, the rise and fall in smoking prevalence was followed by a rise and recent decline in cancer rates. In females, the later rise in smoking prevalence has been accompanied by a rise in cancer rate. A

recent slight decline in smoking rate among females has been associated with a slowing of the rise in cancer rate. Results have been published.

Project Dates:
March 1982–1983.

Reference:
Weiss, W.; Benarde, M.A. "The Temporal Relation Between Cigarette Smoking and Pancreatic Cancer." *American Journal of Public Health* 73(12):1403-1404, December 1983.

1391. PENNSYLVANIA STATE UNIVERSITY, COLLEGE OF MEDICINE, Department of Pathology, Hershey, Pennsylvania 17033.

Project Title:
Mental Development of Children Whose Mothers Smoked During Pregnancy.

Principal Investigators:
Naeye, R.L.; Peters, E.C.

Objective:
To determine whether or not mother's smoking during pregnancy affects the mental development of the child.

Methods or Approach:
Data from the Collaborative Perinatal Study, set up to identify fetal, intrapartum, and neonatal events that affect children's development, and which followed prospectively the course of over 50,000 pregnancies between 1959 and 1966, were well suited for study purposes. Many confounding variables were controlled by multiple regression analysis and by intrapair comparisons of siblings whose mothers had smoked during one but not in the other of two pregnancies.

Results to Date:
Hyperactivity, short attention span, and lower scores on spelling and reading tests were more frequent among children whose mothers had smoked throughout pregnancy. Cognitive abnormalities were mild, with achievement test scores only 2 to 4 percent lower in children of smokers. Behavioral abnormalities in children of smokers were associated with elevated neonatal hemoglobin levels and low birth weights, suggesting that fetal hypoxemia may possibly contribute to the genesis of behavioral abnormalities. The number of children analyzed (at 7 years of age) was 6,492.

Financial Support:
Pennsylvania Hospital Insurance Co.; Michigan Hospital Association Mutual Insurance Co.; Pennsylvania Medical Society Insurance Co.

Reference:
Naeye, R.L.; Peters, E.C. "Mental Development of Children Whose Mothers Smoked During Pregnancy." *Obstetrics and Gynecology* 64(5):601-607, November 1984.

1392. PENNSYLVANIA STATE UNIVERSITY, HERSHEY MEDICAL CENTER, Hershey, Pennsylvania 17033.

Project Title:
Opioid Peptides and the CNS Regulation of Hydration.

Principal Investigator:
Summy-Long, J.Y.

Objective:
To investigate the physiological importance of regulation by opioid peptides of oxytocin and vasopressin release from the hypothalamo-neurohypophysial system.

Methods or Approach:
Concentrations of oxytocin and vasopressin in plasmin, hypothalamus, and neurointermediate lobe of the pituitary are determined in animals pretreated with saline or the opiate receptor antagonist naloxone after stimulation of neurohypophysial hormone release by (1) dehydration, (2) hemorrhage, (3) nicotine, (4) histamine, (5) carbachol, (6) elevation in NaCl in cerebrospinal fluid, (7) parturition, and (8) lactation. The last two stimuli release oxytocin selectively. Vasopression and oxytocin are extracted from plasma and brain tissue and quantified by radioimmunoassay.

Results to Date:
Opioid peptides inhibit release of oxytocin and thereby promote preferential release of vasopressin from the hypothalamo-neurohypophysial system when it is physiologically important to correct fluid imbalance during dehydration and hypotension associated with hemorrhage. Opioid peptides also appear to attenuate release of oxytocin during lactation and parturition in the rat. This inhibition may function to conserve pituitary stores of oxytocin and prevent neuronal fatigue.

Future Plans:
Pharmacologic stimuli (nicotine, histamine, carbachol) will be used to determine if, when, and at which anatomical sites opioid peptides modulate release of oxytocin and vasopressin from the hypothalamo-neurohypophysial system, in vivo and in vitro.

Project Dates:
June 1984–May 1987.

Financial Support:
NHLBI (1R01HL32826-01).

1393. PENNSYLVANIA STATE UNIVERSITY, University Park, Pennsylvania 16802.

Project Title:
Longitudinal Perspectives on Drug Use: Analyses From the New York Longitudinal Study.

Principal Investigators:
Vicary, J.R.; Lerner, J.V.

Objective:
To determine the relationship between various early childhood and adolescent emotional and adjustment characteristics and later use of tobacco, alcohol, and marijuana.

Methods or Approach:
Subjects were 133 white, middle-class children (66 males, 67 females) from the New York Longitudinal Study core sample. They were predominantly Jewish and from New York City and surrounding areas. Data collection began in 1956 and is continuing. The sample has remained intact and a wealth of data exists for each subject. Multiple regression analyses were used and included as criterion variables use of tobacco, alcohol, and marijuana at ages 10 to 13, 13 to 16, 16 to 19, and over 19 years of age.

Results to Date:
Results indicated that characteristics such as high amounts of dissatisfaction and undercompliance at 1 to 6 years of age were related to high amounts of tobacco use at 10 to 13 years of age. Problems with coping and discipline at age 5 were associated with high levels of alcohol use in young adulthood, and marijuana use at ages 13 through 16. During adolescence, problems with emotional expressiveness, self-evaluation, school and social functioning, and implementation of goals were related to high levels of tobacco and marijuana use from age 16 into adulthood, and alcohol use from age 19 on. Design and timing of future prevention efforts should take into account such findings to produce a more holistic, rather than substance-specific, approach, targeting a range of developmental difficulties and outcomes.

Financial Support:
John D. and Catherine T. MacArthur Foundation; NIDA.
Reference:
Vicary, J.R.; Lerner, J.V. "Longitudinal Perspectives on Drug Use: Analyses From the New York Longitudinal Study." *Journal of Drug Education* 13(3):275-285, 1983.

1394. PENNSYLVANIA STATE UNIVERSITY, University Park, Pennsylvania 16802.

Project Title:
Difficult Temperament and Drug Use: Analyses From the New York Longitudinal Study.

Principal Investigators:
Lerner, J.V.; Vicary, J.R.
Objective:
To examine the role of the Thomas and Chess conceptualization of "difficult" temperament (behavioral style) and tobacco, alcohol, and marijuana use.
Methods or Approach:
Subjects were 133, middle-class children (66 males, 67 females) from the New York Longitudinal Study sample. Data collection began in 1956 and is continuing. Substance use data were self-report information from two interviews (early adolescence and late adolescence/young adulthood). Temperament and behavioral style was measured at five points in time (age 1, 3, and 5, and in adolescence and young adulthood). Temperament scores were obtained by rating descriptions of behavior contained in parental interviews (ages 1 and 3), parent and teacher interviews (year 5), and subject interviews in adolescence and young adulthood. Signs of the difficult child (also scored) were low rhythmicity, low adaptability, withdrawal responses, negative mood, and high intensity of reactions.
Results to Date:
Results indicate that possession of difficult temperamental characteristics at age 5 and in early adulthood are associated with tobacco, alcohol, and marijuana use in young adulthood. In addition, use of marijuana throughout adolescence and alcohol and tobacco use from 13 to 16 years of age were related to subject's difficult temperament characteristics in young adulthood. It appears that use of substances (particularly marijuana) in early, middle, and late adolescence is a consistent predictor of difficult temperament in adulthood.
Financial Support:
John D. and Catherine T. MacArthur Foundation; NIDA.
Reference:
Lerner, J.V.; Vicary, J.R. "Difficult Temperament and Drug Use: Analyses From the New York Longitudinal Study." *Journal of Drug Education* 14(1):1-7, 1984.

1395. PHILADELPHIA DEPARTMENT OF PUBLIC HEALTH, Coordinating Office for Drug and Alcohol Abuse Programs, 841 Chestnut Street, Philadelphia, Pennsylvania 19107. SHALOM, INC., 311 South Juniper Street, Philadelphia, Pennsylvania 19107.

Project Title:
HERR Project for Smoking Deterrence Among High Risk Youth.

Principal Investigators:
Allen, W.A.; Strum, B.
Objective:
To (1) provide health education about smoking to students in public and parochial schools; (2) heighten community awareness of the health consequences of smoking; (3) network with other agencies having smoking deterrence goals; and (4) study the epidemiology of smoking (i.e., how an individual's smoking habit influences others of the same family and social circle).
Methods or Approach:
Within school settings, the program includes direct educational presentations to students, seminars for parents, training for teachers, and cross-age peer group discussions via the teacher training segment. Student miniprojects, films, tapes, smoking cessation clinics, and demonstrations are included. In 1984-1985 a special segment on the health hazards of marijuana smoking was added to the sixth grade curriculum. In community settings, health education sessions are held for health practitioners and interested community groups. Preventive and educational efforts have placed emphasis on women, who are now smoking at a higher rate than men and are experiencing an alarming increase in physiological damage associated with smoking. The problem is compounded for pregnant women, considering the health hazards for the fetus. Educators in the project function as referral resources for smoking cessation groups and related services. As data are collected, a more comprehensive smoking and health program can be planned for Philadelphia, which could provide a model for similar projects throughout the nation.
Results to Date:
In the first year, more than 10,000 students learned about the dangers of smoking, and more are benefiting from the project in its second year (October 1984-September 1985). Emphasis is on fifth and sixth grade students since this is the age when many start to smoke. More than 500 seventh graders are scheduled to participate in the "Keep It Clean" curriculum in the second year. The project is also being expanded to include community groups and private industry. North Philadelphia and other economically depressed areas are the current target areas.
Future Plans:
Results will be analyzed and subjective data on smoking beliefs, attitudes, and behaviors will be studied, based on pre- and posttest questionnaires. Epidemiological effects will also be analyzed.
Financial Support:
Pennsylvania Department of Health.

1396. PREVENTION RESEARCH CENTER, Rodale Press, Inc., 33 East Minor Street, Emmaus, Pennsylvania 18049.

Project Title:
The Prevention Index.

Principal Investigators:
Irvine, S.; Bausell, R.B.; Taylor, H., et al.
Objective:
To provide Americans with a yearly yardstick to measure the Nation's progress in achieving better health and less dependence on an increasingly expensive medical system.
Methods or Approach:
The index is designed to find out what Americans are doing to stay healthy and how much potential remains in the American way of life for additional prevention to occur. The system assesses the Nation's efforts toward achieving a positive health strategy by measuring the behaviors or actions taken by people in areas well recognized as affecting disease and disability. It pinpoints specific preventive steps that Americans need to take to achieve maximum health potential and highlights accomplishments over the past year. The index is developed from information collected by Louis Harris and Associates, Inc., in two national surveys: (1) self-reports of compliance with 21 health-seeking behaviors based on a random sample of 1,254

members of the continental United States population; and (2) ratings of the importance of each of the behaviors with respect to their impact on the overall health of the general population as determined by a sample of 103 representative experts in disease prevention and health promotion. The index is keyed to a base of 100, defined as 100 percent of the adult population of the United States engaging in all of the 21 key health-seeking behaviors. The actual computation of the index was accomplished by (1) multiplying the percentage of the adult population who reported engaging in each health-seeking behavior by the appropriate experts' rating; (2) adding the 21 products together; and (3) adjusting the resulting total to a scale of 100 (which would indicate 100 percent compliance with all 21 behaviors). The behaviors covered include exercise and weight control, diet and nutrition, smoking and alcohol use, safety precautions, stress management, medical exams, and other preventive behaviors.

Results to Date:

In its first year measurement, the index places the American public at 61.5 percent in its efforts to achieve good health. Of the key preventive measures studied, the average adult practices more than half. The groups most likely to be prevention oriented are older people, women, those with higher incomes, persons in professional or managerial occupations, those who state that they are in excellent health, and people who feel that they have a great deal of control over their future health. Concerning smoking, 70 percent of adults say they do not smoke and 30 percent say they do; this is the lowest smoking rate and the highest nonsmoking rate ever recorded in a Harris survey. The 103 experts rated nonsmoking as the number one preventive health priority for adults. Groups with the highest percentage of nonsmokers were older people, college graduates, and those in the higher income brackets. However, differences among various demographic groups are not very strong. A striking finding is that the rate of smokers vs. nonsmokers among women today is approximately equal to the rate among men, continuing a trend toward convergence. However, 8 of 10 mothers say that they did not smoke during pregnancy, and although many had been smokers, 18 percent had expressly stopped during pregnancy and were classified as nonsmokers.

Future Plans:

Research for the second annual index has been completed and new data will be released in May 1985. Plans are to make the index an annual project.

Project Dates:

March 1983–continuing.

Reference:

Prevention Research Center. *The Prevention Index. A Report Card on the Nation's Health.* Rondale Press, (undated), 26 pp.

Financial Support:

Prevention Research Center.

1397. STUDIES ON SMOKING, 125 High Street, Edinboro, Pennsylvania 16412.

Project Title:

Longevity of Nonsmoking Men and Women: A Demographic Study in Erie County.

Principal Investigator:

Miller, G.H.

Objective:

To study the effect of nonsmoking on longevity in males vs. females.

Methods or Approach:

Retrospective data for 2,195 deceased lifetime nonsmokers were combined with telephone survey data on lifetime smoking habits (with careful distinctions between former smokers and never smokers) of 3,196 residents of Erie County, Pennsylvania, aged 30 or over.

Results to Date:

Results imply that sex role behavior among males (i.e., excessive smoking, alcohol consumption, disdain for minor medical assistance, and suicidal and accident-risk tendencies) affect health, morbidity, and longevity, and that female health and morbidity will suffer as their behavior trends become increasingly similar to trends among males. Smoking is increasing among females, and teenage rates are higher for females than for males. When women who have smoked as much as men reach the later decades of life, their lives may also be shortened, eliminating present differences in longevity. Study results have been published.

Financial Support:

National Academy of Science.

Reference:

Miller, G.H.; Gerstein, D.R. "The Life Expectancy of Nonsmoking Men and Women." *Public Health Reports* 98(4):343-349, July-August 1983.

1398. STUDIES ON SMOKING, 125 High Street, Edinboro, Pennsylvania 16412.

Project Title:

Male–Female Longevity Comparisons Among the Amish.

Principal Investigator:

Miller, G.H.

Objective:

To compare the incidence of lung cancer between the Amish and non-Amish populations in Lancaster County, Pennsylvania.

Methods or Approach:

Cancer mortality data from Lancaster County, Pennsylvania, were analyzed for incidence of lung cancer mortality in the Amish (n = 12,000 in 1977) and non-Amish (n = 337,500 in 1977) populations.

Results to Date:

Analysis showed 1 lung cancer death among the Amish compared with 348 lung cancer deaths among non-Amish county residents, verifying that a nonsmoking population has a low incidence of lung cancer. The single Amish lung cancer death was a cigar smoker; there were no lung cancer fatalities among Amish nonsmokers. Lung cancer incidence in smokers compared with nonsmokers in a merged population, containing both smokers and nonsmokers, is 10 to 1. Since there were no reported lung cancer cases for the nonsmoking Amish population, incidence is lower than would be expected after making adjustments for a nonsmoking merged population. It is suggested that the lower incidence is due to the smoke-free Amish environment, where nonsmokers are not subjected to second-hand smoke (passive smoking).

Project Dates:

October 1976–continuing.

Reference:

Miller, G.H. "Lung Cancer: A Comparison of Incidence Between the Amish and Non-Amish in Lancaster County." *Journal of the Indiana State Medical Association* 76(2):121-123, February 1983.

1399. STUDIES ON SMOKING, 104 Valley View Drive, Edinboro, Pennsylvania 16412.

Project Title:

Pennsylvania Physicians' Study on Smoking and Health.

Principal Investigator:
Miller, G.H.
Objective:
To determine the impact of smoking on a complete population of physicians; compare the population from the Pennsylvania Physicians' Study with that of the Northwestern Pennsylvania Study on Smoking and Health (Erie County).
Methods or Approach:
Close relatives of deceased physicians were interviewed to determine the decedents' smoking habits. Information on amount of cigarette smoked, length of cigarette smoked, family smoking habits, diseases of the deceased, and cause of death were obtained. The data will be analyzed for patterns in life expectancy between the smoker and nonsmoker, as well as differences in diseases, family smoking patterns, and other important comparisons between smokers and nonsmokers which arise as the data are analyzed.
Results to Date:
Preliminary results show that nonsmokers live much longer than their smoking counterparts.
Future Plans:
The study may be expanded to other States.
Project Dates:
September 1977–continuing.

1400. STUDIES ON SMOKING, 104 Valley View Drive, Edinboro, Pennsylvania 16412.

Project Title:
Carbon Monoxide Studies.

Principal Investigator:
Miller, G.H.
Objective:
To (1) determine the carbon monoxide exhalation levels of smokers, nonsmokers, and those who are in the process of quitting smoking; (2) assess the pattern of carbon monoxide concentration at different times during the day in selected buildings; and (3) compare carbon monoxide levels in smokers and nonsmokers with varying exposure levels.
Methods or Approach:
The approximate level of carbon monoxide exhaled by the smoker and nonsmoker is measured by an Ecolyzer. A number of different buildings have been checked at different times during the day to determine different concentrations in carbon monoxide levels. Groups of smokers and nonsmokers have been measured for exhalation under different concentrations of carbon monoxide.
Results to Date:
Nonsmokers have been shown to have a very small amount of carbon monoxide exhalation ranging from 0.5 to 2.0 ppm. Smokers in general have much higher levels, ranging from 6 to 72 ppm.
Project Dates:
January 1977–continuing.

1401. STUDIES ON SMOKING, 104 Valley View Drive, Edinboro, Pennsylvania 16412.

Project Title:
SOS Stop Smoking Clinics.

Principal Investigator:
Miller, G.H.
Objective:
To maximize the success rate of smokers in quitting smoking permanently.
Methods or Approach:
The 1-year program consists of a minimum of 15 sessions of lectures, films, and group counseling. The program uses the latest techniques in behavior modification, including the "Reverse Peer Pressure System" and the "Buddy System." The participants receive individualized counseling from the director to aid them with their specific problems. Behavior patterns and carbon monoxide exhalation are recorded to enable a more complete analysis of methods to improve the success rate for smokers in making them nonsmokers.
Results to Date:
The success ratio has varied, with a success rate for Erie County approaching 60 percent at the end of the year. A recent clinic at Cummins Engine Company reported a success rate of 70 percent in 4.5 months and 55 percent at the end of the year.
Future Plans:
Reports will be made on carbon monoxide exhalation of those who stop smoking, patterns of behavior during the withdrawal period, and other relevant information observed during the cessation process.
Project Dates:
August 1975–continuing.

1402. STUDIES ON SMOKING, 104 Valley View Drive, Edinboro, Pennsylvania 16412.

Project Title:
Northwestern Pennsylvania Study on Smoking and Health.

Principal Investigator:
Miller, G.H.
Objective:
To (1) determine the impact of cigarette smoking on the longevity differences between men and women; (2) assess the effect of different amounts of smoking; (3) elucidate different disease patterns in smokers vs. nonsmokers; and (4) examine the effect of smoking on family and spouses.
Methods or Approach:
Clerical assistants search death notices of the *Erie Times* and identify relatives that are locatable. Those who are locatable are entered on an interview form which is given to the interviewers for completion. Data on smoking habits are obtained from close relatives of the deceased by means of telephone interviews. The data will be analyzed for sex differences, effect of smoking on families and spouses, differences in disease patterns, and effects of different amounts of smoking.
Results to Date:
There is practically no difference in longevity between men and women if they do not smoke cigarettes or work in industries with pollutants. The longevity difference in favor of the nonsmoker over the smoker is greater than 10 years. The longevity difference for the heavy smoker compared to the nonsmoker ranges from 14 to 15 years for men to 19 to 20 years for women. Smoking of pipes and cigars does not appear to have any effect on longevity.
Future Plans:
Plans are being made for extension of the northwestern Pennsylvania study to a longitudinal study in this area, in other areas of Pennsylvania, and in the nation.
Project Dates:
May 1974–continuing.

1403. STUDIES ON SMOKING, 125 High Street, Edinboro, Pennsylvania 16412.

Project Title:
Cancer, Passive Smoking and Nonemployed and Employed Wives.

Principal Investigator:
Miller, G.H.
Objective:
To determine the relationship between cancer and passive smoking in nonemployed and employed wives.
Methods or Approach:
Data on cause of death, smoking history, and other relevant information were obtained in Erie County, Pennsylvania, in 1975-1976. Nonsmoking wives (n=547) were classified by husband's smoking history and their own employment outside the home.
Results to Date:
Mortality due to cancer showed an almost twofold increase among nonemployed wives with long-term exposure to passive smoking compared with nonemployed wives who experienced little or no exposure. There was a highly positive, but not statistically significant, association between long-term passive smoking and cancer as a cause of death for the entire group. The odds ratio was 0.40 and the X^2 value was 2.18 for all wives. When women working outside the home were omitted, the odds ratio reached significance at 1.94. When working wives were included, the odds ratio for women aged 59 and younger was high and statistically significant. Findings support the hypothesis that long-term passive smoking leads to excess cancer deaths in exposed nonsmokers. For employed wives, the fact that husbands smoked or did not smoke seemed unimportant, probably because of exposure to smoke and other hazards in the workplace. Results have been published.
Reference:
Miller, G.H. "Cancer, Passive Smoking and Nonemployed and Employed Wives." *Western Journal of Medicine* 140(4):632-635, April 1984.

1404. TEMPLE UNIVERSITY, Department of Chemistry, Philadelphia, Pennsylvania 19122.

Project Title:
Electroanalytical Studies on N-Nitrosamines.

Principal Investigator:
Harrington, G.W.
Objective:
To develop analytical procedures, both quantitative and qualitative, for the detection and determination of N-nitrosamines in various biological media, with emphasis on electroanalytical techniques, including electrochemical detection for high performance liquid chromatography (HPLC); study the metabolism of N-nitrosamines and the chemistry of N-nitrosamines, especially that chemistry related to the formation and destruction of N-nitrosamines.
Methods or Approach:
Nitrosamines are studied by class (e.g. volatile, nonvolatile) using differential pulse polarography and HPLC with an electrochemical detector (polarographic detector). Model solutions are used to establish the required experimental parameters and then biological matrices are used, such as blood, urine, saliva or tissues. When the procedures for the biological matrices are established, in vivo experiments are conducted using laboratory animals.
Results to Date:
Methods have been developed for approximately 50 nitrosamines using either differential pulse polarography or HPLC-EC. The methods have been shown to be reliable in blood, serum, urine, and tissue. Methods have also been developed for nitrosamine precursors such as nitrite and nitrate. This has been shown to be useful in a variety of matrices including human saliva. Studies have also been completed on the role of vitamin C in the formation and destruction of nitrosamines. In most instances vitamin C inhibits the formation of nitrosamines, but in a few instances it accelerates their formation. Metabolism studies in the rat have been conducted for dimethylnitrosamine and N-nitroso-N-methylaniline.
Future Plans:
Analytical methods suitable for large-scale screening of various commercial products and for human exposure will be developed. There will be an increased emphasis on in vivo studies designed to elucidate the metabolic pathway for various nitrosamines and the routes of absorption into the circulatory system.
Project Dates:
June 1980–1983.
Financial Support:
NCI (5R01CA18618).

1405. TEMPLE UNIVERSITY, SCHOOL OF DENTISTRY, Department of Operative Dentistry, Philadelphia, Pennsylvania 19140.

Project Title:
Chemical Studies on Chewing Tobacco in Relation to Oral Health.

Principal Investigator:
Hsu, S.C.
Objective:
To identify carcinogenic sugars in commercial available nonsmoking tobaccos.
Methods or Approach:
Representative samples of each of the forms of commercially available nonsmoking tobacco were analyzed (loose-leaf pouches, pressed-plug form tobacco, and powdered snuff tobacco). Oven-dried tobacco samples were ground and stirred in water to obtain water-soluble extracts. TMS sugar derivatives were used for gas liquid chromatographic analysis; high pressure liquid chromatography was used to confirm results of gas liquid chromatographic analysis.
Results to Date:
A typical pouch tobacco (Red Man) contained 9.2 percent sucrose, 3.9 percent glucose, 1.3 percent fructose, and 1.4 percent maltose; a plug tobacco (Day-O-Work) contained 1.9 percent sucrose, 2.8 percent glucose, 5.8 percent fructose, and no detectable maltose. The snuff tobacco tested (Copenhagen) contained 7.4 percent fructose, but no other sugars were detected.
Future Plans:
The correlation of sugar content in chewing tobacco to dental caries incidence will be investigated, since mechanical chewing, chemical action, and biological effects of the extracted tobacco juice may have significant effects on oral health.
Project Dates:
March 1980–continuing.
Financial Support:
Temple University (700-052-24).

1406. TEMPLE UNIVERSITY, SCHOOL OF MEDICINE, Department of Psychology, Weiss Hall, 13th Street and Columbia, Philadelphia, Pennsylvania 19122.

Project Title:
Basic Mechanisms of State Dependent Learning.

Principal Investigator:
Overton, D.A.

Objective:
To (1) develop improved methods for studying subjective effects of drugs in animals; (2) improve understanding of pharmacological and psychological mechanisms that allow animals to discriminate subjective drug effects; and (3) increase utility of such drug discrimination procedures as methods for studying neuropharmacological actions and interactions of centrally acting drugs.

Methods or Approach:
The project does not specifically focus on nicotine, but most results obtained and procedures developed will be applicable to nicotine, since it is a readily discriminable drug. Rats are trained to bar press to obtain water reinforcement in training compartments containing two levers. Before training sessions, either drug or saline is injected and rats are reinforced for pressing lever 1 during sessions when they are drugged, and for pressing lever 2 during sessions when they are undrugged. After 20 to 50 sessions, animals learn to press only the lever that is appropriate to the currently imposed drug condition, and drug discrimination is said to have been learned; test sessions can then be conducted. Before each test session, a novel drug or dosage is injected. Data collected during test sessions indicate the degree of perceived similarity between subjective effects of the test drug condition and those of the training drug condition. Experiments are underway in which details of the training procedures or the drugs employed are being varied to (1) improve speed and/or efficiency of the drug discrimination procedure; (2) improve quality of data obtained; (3) evaluate relative importance of drug-induced sensory cues and "no drug" cues as agents controlling discriminative behavior; and (4) use the discrimination procedure to answer specific questions about the discriminable effects of selected drugs.

Results to Date:
Several new behavioral procedures have been identified that increase the speed at which drug discriminations are learned and allow the investigator to control the degree of specificity produced by the training procedure. The relative degree of discriminability of a variety of centrally acting drugs have been measured and it has been determined that nicotine is readily discriminated.

Future Plans:
An attempt will be made to appraise the ability of drugs, including nicotine, to act as conditioned stimuli in classical conditioning paradigms. If drugs can act as conditioned stimuli, consistent pairing of drug administration with an environmental event could establish a conditioned response to the drug that would essentially constitute a new (temporary) drug effect.

Project Dates:
June 1975–March 1986.

Financial Support:
NIMH (R01MH25136).

1407. THE GRADUATE HOSPITAL, RESEARCH DIVISION, Department of Medicine, One Graduate Plaza, Philadelphia, Pennsylvania 19146.

Project Title:
Oxidant Effects on Elastase and Alpha-1-Protease Inhibitor.

Principal Investigator:
Weinbaum, G.

Objective:
To determine the sequence of events occurring after oxidant exposure that causes an alteration in alpha-1-proteinase inhibitor:elastase balance in the lung; establish whether the imbalance generates an increase in available elastase.

Methods or Approach:
Oxidants used include the defined oxidants chloramine-T and nitrogen dioxide (NO_2), and the complex mixture of oxidants found in cigarette smoke. Biochemical, immunological, and ultrastructural analyses of lung components from oxidant-exposed and control animals are used to measure functional and oxidized (inactive) proteinase inhibitor and the effect of oxidant dose and exposure duration on components. Effect of oxidant exposure on cell populations in the lung are also analyzed, with particular emphasis on elastase release. Immunolocalization is used to determine if oxidant exposure causes accumulation of interstitial elastase in the alveolar wall.

Results to Date:
Long-term exposure to cigarette smoke or NO_2 caused pulmonary emphysema. In addition, in the dog model, within 1 hour after smoking three cigarettes, there was an influx of neutrophils into the airways that continued for 12 to 16 hours after cessation of smoking. Neutrophils obtained by lavage after smoking had lost much of their elastase, probably by degranulation during migration into the lung. Ultrastructural immunolocalization of human neutrophil elastase in the alveolar interstitium of human emphysematous lungs was successful. In the NO_2-exposed rat model, neutrophil influx and degranulation occurred.

Future Plans:
To determine if released elastase is effectively digesting alveolar wall elastin, hydrolysis products of elastin digestion will be quantitated immunologically in lavage fluid and plasma of oxidant-exposed animals.

Project Dates:
January 1983–December 1985.

Financial Support:
NHLBI (HL 29734-03).

1408. UNIVERSITY OF PENNSYLVANIA HOSPITAL, CARDIOVASCULAR SECTION, 654 Ravdin Building, 3400 Spruce Street, Philadelphia, Pennsylvania 19104.

Project Title:
Effect of Nicotine on Coronary Blood Flow.

Principal Investigators:
Martin, J.L.; Laskey, W.K.

Objective:
To determine the effect of nicotine on coronary blood flow relative to myocardial oxygen demand.

Methods or Approach:
Prior studies demonstrated that cigarette smoke had a vasoconstrictive effect on coronary circulation; the present research is to determine if this effect is due specifically to nicotine as opposed to other components in cigarette smoke. Coronary sinus blood flow is measured by thermodilution, and myocardial O_2 delivery is calculated by multiplying flow times the

transmyocardial AV O_2 difference. Myocardial lactate extraction is also determined. Parameters are remeasured during incremental atrial pacing. After administering nicotine as Nicorette gum, the protocol is repeated. Coronary flow, coronary resistance, myocardial O_2 uptake, and myocardial lactate extraction are compared pre- and postnicotine exposure at equivalent double products.

Results to Date:
Project is in a preliminary phase.

Project Dates:
December 1985–December 1986.

Financial Support:
University of Pennsylvania Hospital.

1409. UNIVERSITY OF PENNSYLVANIA, JOHNSON FOUNDATION, D-501 Richards, Philadelphia, Pennsylvania 19104.

Project Title:
Human Breath and Tissue Spontaneous Chemiluminescence–Clinical and Chemical Correlations.

Principal Investigators:
Williams, M.D.; Chance, B.

Objective:
To characterize the mechanisms and emitters of breath and tissue luminescence; determine clinical usefulness of breath and tissue luminescence measurements is assessing status and progress of disease and therapy.

Methods or Approach:
Breath and/or tissue luminescence is measured from unperturbed subjects using a photon counter. Chemical contents of gaseous and liquid phases of the imaged material are analyzed by routine means. Correlations between chemical content and physiological condition of the subject and chemiluminescence intensity, spectra, intensity fluctuation, and statistical properties are examined.

Results to Date:
Some correlation with peroxide content of breath and luminescence intensity was found. Lung tissue luminescence was correlated to breath luminescence intensity. Cigarette smoking intensified breath luminescence. Breath luminescence intensity decreased very slowly in samples trapped in balloons. Luminescence of hand, head, and chest was of lower intensity than that of mouth or lung.

Future Plans:
Clinical studies to include oxygen therapy patients, exercise and fatigue studies in normal subjects, and several other chemical correlation studies are planned. The time course of disease and treatment in several patient populations will be examined.

Project Dates:
February 1981–continuing.

Financial Support:
NHLBI (SCOR-HL-15061).

1410. UNIVERSITY OF PENNSYLVANIA, THE WHARTON SCHOOL, Department of Statistics, Philadelphia, Pennsylvania 19104.

Project Title:
Epidemiological Studies on Relationships of Air Pollution, Smoking, Ionizing Radiation and Other Variables to Human Chronic Disease Mortality.

Principal Investigators:
Hickey, R.J.; Clelland, R.C.

Objective:
To test hypotheses that (1) some common air pollutant chemicals are hazardous to health, some harmless, and others beneficial; (2) chronic disease development is influenced by genetic/constitutional characteristics; (3) some characteristics influence certain behavioral characteristics such as drinking of coffee, tea, or alcoholic beverages, cigarette smoking, and other behaviors; (4) smoking and/or coffee drinking may be symptomatic of physiological deficiencies that nicotine and/or caffeine tend to alleviate; (5) unalleviated deficiencies contribute to increased risk of unrepaired genetic damage, insufficient bioenergetics for efficient defense mechanisms, and increased risk of mortality from chronic diseases such as cancer; (6) viruses contribute to risk of chronic diseases, especially in the presence of bioenergetic deficiency; (7) traces of nonnutrient toxic chemicals can function as hormetic stimulants; (8) low levels of ionizing radiation are stimulatory and beneficial rather than damaging; (9) a few individuals, genetically deficient in DNA repair and in other repair capabilities, incur elevated risks of cancer, leukemia, and certain other chronic diseases from environmental variables such as natural radiation, viruses, and certain chemicals; and (10) in an epidemiological situation, a correlation, no matter how strong, is incapable of distinguishing cause from symptom.

Methods or Approach:
Multiregional data sets (43 cities and 48 states) are being investigated. An optimal subset selection (algorithm) modification of multiple regression analysis continues to function well for complex systems analyses. Data used are environmental, vital statistical, and socioeconomic. Diseases of interest are various cancers, leukemias, cardiovascular diseases, birth defects, and other chronic problems as reported for the various regions. Foundations to explain the biostatistical findings are sought in biochemistry, biology, evolutionary biology, population biology and population genetics, and biochemical ethology. An ethological and evolutionary biological concept under examination is that of species-preserving habituation, which could involve behavioral regulation of physiological homeostasis that, when effective, would tend toward maintenance of near optimal internal homeostatic characteristics.

Results to Date:
Results have generally been consistent with the hypotheses and theories noted. Environmental chemical concentrations continue to be strongly correlated with mortality rates for various categories of cancer; certain socioeconomic variables are strongly correlated with mortality rates; and explained variances in mortality rates for various regions are about 50 to 80 percent, including cancer of the respiratory organs.

Future Plans:
Investigations will continue with emphasis on developing evidence and understanding of the chemical hormesis phenomenon and on the likelihood that nicotine is an hormetic chemical that contributes to optimal ethological homeostatic maintenance for smokers. In addition, the relationship of bioenergetic deficiency to immunology and to virus vulnerability will be measured.

Project Dates:
1967–continuing.

Financial Support:
CTR.

References:
(1) Hickey, R.J.; Allen, I.E. "Surgeons General's Reports on Smoking Cancer: Uses and Misuses of Statistics and of Science." *Public Health Reports* 98(5):410-411, 1983. (2) Bowers, E.J.; Allen, I.E.; Hickey, R.J. "Cigarette Smoking: Example of Behavioral Regulation of Physiological Homeostasis?" *Public Health Reports* 99(2):108-110, 1984. (3) Hickey,

R.J.; Bowers, E.J.; Spence, D.E., et al. "Low Level Ionizing Radiation and Human Mortality: Multi-Regional Epidemiological Studies. A Preliminary Report." *Health Physics* 40:625-641, 1981. (4) Hickey, R.J.; Bowers, E.J.; Clelland, R.C. "Radiation Hormesis, Public Health, and Public Policy: A Commentary." *Health Physics* 44:207-219, 1983. (5) Luckey, T.D. "Physiological Benefits From Low Levels of Ionizing Radiation." *Health Physics* 43:771-789, 1982. (6) Hickey, R.J.; Bowers, E.J.; Allen, I.E. "Statistical Fantasy." *Nuclear News* 25(14):49-50, 52, 1982. (7) Hickey, R.J. "Risks Associated With Exposure to Radiation: Science, Pseudoscience and Opinion." *Health Physics* (in press). (8) Bowers, E.J.; Hickey, R.J.; Junker, L.L., et al. "Biosocial Factors in Infant Mortality: Multivariate Analysis of Rates of Births, Lethal Congenital Defects, and Infant Mortality." In: Broms, J.; Hauspie, R.; Sand, A., et al. (Editors). *Human Growth and Development.* New York, Plenum Press, 1984, pp. 71-76.

1411. UNIVERSITY OF PENNSYLVANIA, 133 South 36th Street, Suite 507, Philadelphia, Pennsylvania 19104.

Project Title:
Cardiovascular Risk Reduction of Parents and Children.

Principal Investigator:
Brownell, K.D.
Objective:
To implement and evaluate a comprehensive educational program in the schools to alter the cardiovascular "at-risk" behavior of children and their parents.
Methods or Approach:
The program is designed to prevent children from developing behavior patterns that might result in heart disease as adults and to alter the current behaviors of children and adults that are believed to result in heart disease. It is felt that a comprehensive risk factor program aimed at both parents and children is likely to have an impact beyond the initial point of intervention, i.e., that changes will be sustained over time. Risk factors to be addressed include smoking, nutrition, and blood pressure management. All interventions are based on social learning theory and are designed to be delivered by older children who should be good role models for the children receiving the program. Programs to be conducted are adaptations of programs of known efficacy and will include additional evaluation and modification of the programs to be delivered by peers, direct instruction of parents, and training of children to talk with their parents about health behavior.
Results to Date:
Project is in a preliminary phase.
Project Dates:
1984–June 1987.
Financial Support:
NHLBI (1R18HL30576-01).

1412. UNIVERSITY OF PENNSYLVANIA, Department of Biochemistry and Biophysics, D501 Richards/G4, Philadelphia, Pennsylvania 19104.

Project Title:
Instabilities of Cardiac Myopathies.

Principal Investigator:
Chance, B.
Objective:
To establish conditions of cardiac hypoxia that lead to unstable metabolic control with tendencies toward heart failure.
Methods or Approach:
Beagle dog hearts are studied by phosphorus nuclear magnetic resonance using a surface coil implanted to a left thoracotomy. Results are rated with respect to respiration and heartbeat. All physiological parameters (electrical and circulatory) are measured.
Results to Date:
Energy states of the heart in terms of phosphocreatine (PCr) and phosphate (P_i) ratio have been identified. Results indicate that the heart stabilizes itself through autoregulation of values that are relatively high compared with the brain (over 5 compared with 1 or 2) and during hypoxic stress, the heart (through close-knit autoregulatory feedback) maintains this energy state until "heart failure." Under such conditions, coronary profusion fails and the energy state rapidly falls to an unstable level, leading to lactic acidosis, ionic equilibration, and cell damage. The studies afford an excellent model for prediction of cardiac problems due to excessive smoking.
Future Plans:
The animal model will be further explored, and when the phosphorus spectrometer becomes available, cardiac problems in humans will be studied.
Project Dates:
September 1983–continuing.
Financial Support:
NHLBI (HR34004, HL06817); AMA (417 62HY).

1413. UNIVERSITY OF PENNSYLVANIA, SCHOOL OF MEDICINE, 37th and Hamilton Walk, Philadelphia, Pennsylvania 19104. CORNELL UNIVERSITY MEDICAL COLLEGE, 525 East 68th Street, New York, New York 10021.

Project Title:
Etiologic Study of Systemic Lupus Erythematosus.

Principal Investigators:
Strom, B.L.; Stolley, P.D.; Reidenberg, M.M.
Objective:
To identify risk factors for idiopathic systemic lupus erythematosus (SLE) and lupus-like illness.
Methods or Approach:
The retrospective case–control study will determine whether patients with SLE who fulfill at least four of the revised American Rheumatism Association criteria for SLE differ in any of the characteristics from patients who have lupus-like illness (patients who meet fewer than four criteria). It is hypothesized that (1) idiopathic SLE or lupus-like illness may be caused by aromatic amines or hydrazines and that (2) individual variation in susceptibility to lupus induction is affected by individual variation in rates of drug acetylation. Nonhospitalized incident and recent prevalent cases of SLE and lupus-like illness will be compared with two sets of controls matched to cases by age and sex. One control group will comprise general medical outpatients. The other will consist of friends of cases. Individuals will be interviewed to obtain information on demographic characteristics, personal medical history, family medical history, previous drug exposures, and exposures to environmental agents, including use of tobacco. Dapsone will be administered and a blood specimen will be collected and analyzed for dapsone and monoacetyldapson, as a measure of acetylator phenotype.
Results to Date:
Results are not yet available.
Project Dates:
April 1984–March 1987.

Financial Support:
NIADDK (1R01AM32869-02).

1414. UNIVERSITY OF PENNSYLVANIA, SCHOOL OF MEDICINE, 37th and Hamilton Walk, Philadelphia, Pennsylvania 19104. PAN AMERICAN HEALTH ORGANIZATION, 525 23rd Street, NW., Washington, D.C. 20037.

Project Title:
Biochemical Epidemiology of Biliary Tract Cancer.

Principal Investigators:
Strom, B.L.; Soloway, R.; Stolley, P.D.
Objective:
To determine whether patients with different primary cancers of the biliary tract differ from each other, from patients with cholelithiasis, and from patients with other abdominal illnesses with respect to parameters obtained through biochemical analysis of specimen data, questionnaires, and medical record abstract completions.
Methods or Approach:
The La Paz Cancer Registry in La Paz, Bolivia, and the Universidad Autonoma in Mexico City, Mexico, are also involved in the study. The case–control investigation of biliary tract cancers will include all newly diagnosed cases of biliary tract cancer and controls selected from abdominal surgery patients at each of five participating hospitals in Latin America. Several biochemical analyses will be performed on sera, bile, and where appropriate, gallstone specimens. The questionnaire will determine demographic characteristics, environmental exposures (including tobacco usage), and prior medical and drug histories. The medical record abstract will validate patient's current medical diagnosis.
Results to Date:
Results are not yet available.
Project Dates:
March 1984–February 1987.
Financial Support:
NCI (R01CA35934-02).

1415. UNIVERSITY OF PENNSYLVANIA, 3600 Spruce Street, Philadelphia, Pennsylvania 19104.

Project Title:
Pulmonary Macrophage Heterogeneity - Humans and Guinea Pigs.

Principal Investigator:
Rossman, M.D.
Objective:
To (1) investigate heterogeneity of alveolar macrophages (AM) from humans and guinea pigs; (2) define populations of AM by density gradient centrifugation; (3) investigate surface changes of AM as defined by monoclonal antibodies; (4) define subpopulations of AM by collecting AM from individuals in a variety of disease states, including normals, smokers, and patients with sarcoidosis; and (5) using the guinea pig model, obtain cells from normal guinea pigs and from those with silicosis or berylliosis.
Methods or Approach:
Percoll gradient separation techniques will be used to define guinea pig and human AM that have different densities. Functional differences among AM will be determined by adherence, spreading, Fc receptor, and accessory cell function; types of surface determinants will be determined by monoclonal antibodies. Effect of various substances on ability to modulate subpopulations of AM will also be detected. Substances to be tested include surfactant, fibronectin, bacterial factors, and N-formyl peptides.
Results to Date:
AM of smokers were heavier than AM of nonsmokers, a difference also seen when AM were obtained from patients with active pulmonary disease such as sarcoidosis. When subpopulations of AM were tested for accessory cell function, no difference was found in ability of AM to act as accessory cell for mitogen proliferation among various subpopulations. However, the more dense cells were better able to act as accessory cell for antigen proliferation. Reasons for this discrepancy are under current investigation. No difference was found between smokers and nonsmokers in ability of AM to act as accessory cells. In addition, Fc receptor activity of monocytes and AM was compared in normal subjects and patients with sarcoidosis. Using monomeric immunoglobin G (IgG), equilibrium binding data were obtained and number and affinity of binding sites for monomeric IgG were calculated. Density of IgG binding sites on monocytes and AM was similar; however, because AM were much bigger cells, they had a much higher number of IgG binding sites. In contrast, monocytes from patients with sarcoidosis had increased density and number of IgG binding sites. It was surprising that AM from patients had normal number and density of IgG binding sites.
Future Plans:
Inability of lighter AM to act as accessory cells for antigen proliferation will be investigated, and measurement of Fc and complement receptors among subpopulations of AM is planned.
Project Dates:
April 1983–March 1986.
Financial Support:
NHLBI (5R01HL31136-02).

1416. UNIVERSITY OF PITTSBURGH, SCHOOL OF PUBLIC HEALTH, A517 Parran Hall, Pittsburgh, Pennsylvania 15261.

Project Title:
Coordinating Center–National Heart, Lung and Blood Institute Type II Coronary Intervention Study (Type II Study).

Principal Investigator:
Detre, K.M.
Objective:
To establish a coordinating center which will manage the processing, analysis, and maintenance of all data on randomized subjects for the Type II Study and the surveillance of data collection to assure adherence to protocol; evaluate the 5-year treatment effect of cholestyramine on low density lipoprotein (LDL) cholesterol and on lesions in the coronary arteries of subjects with Type II hyperlipoproteinemia and coronary artery disease (CAD).
Methods or Approach:
The Type II Study is a double-blind, placebo-controlled clinical trial with 143 participants randomly allocated to a daily dosage of 24 grams cholestyramine and diet (treatment group), or placebo and diet (control group). Changes in the coronary arteries were evaluated by sequential coronary angiography carried out before and after 5 years of treatment.
Results to Date:
Baseline demographic and lifestyle characteristics of study participants are as follows: average age, 46; 80 percent are males, 88 percent are married, 54 percent are college or postcollege educated, 75 percent are in professional or white collar occupations; 21 percent never smokers, 39.9 percent

former smokers, 39 percent present smokers; history of alcoholism, 6.3 percent, 10 or more drinks/week, 30 percent; leisure physical activities more active than others 22 percent, less active 22 percent. Details of the Type II study population have been published.

Future Plans:
Further analyses of the results of the study will include analysis of the characteristics that may be associated with progression of CAD.

Project Dates:
September 1977–1985.

Financial Support:
NHLBI (N01-HI-72947).

Reference:
Detre, K.M. "National Heart, Lung and Blood Institute Type II Coronary Intervention Study: Design, Methods and Baseline Characteristics." *Controlled Clinical Trials* 1982.

1417. UNIVERSITY OF PITTSBURGH, Department of Epidemiology, 130 DeSoto Street, Pittsburgh, Pennsylvania 15261.

Project Title:
Potential Risk Evaluation in Diabetics and Non-Affected Siblings.

Principal Investigator:
Orchard, T.T.

Objective:
To evaluate cardiovascular disease risk factors such as blood pressure, cholesterol, and smoking among diabetic and nondiabetic adolescents.

Methods or Approach:
Information on the participant's family history, alcohol consumption, smoking habits, exercise, and fat consumption was obtained through a questionnaire. Fasting blood work was drawn to evaluate lipid levels and sex hormones. As part of a physical examination, height, weight, blood pressure, and degree of sexual maturation were assessed.

Results to Date:
Frequency of smoking in the diabetic adolescents was low, comparable to the nondiabetic adolescents and unrelated to the lipoprotein profiles and blood pressures in either group.

Project Dates:
October 1981–1983.

Financial Support:
NHLBI; NIAMDD.

1418. UNIVERSITY OF PITTSBURGH, SCHOOL OF PUBLIC HEALTH, Department of Epidemiology, A544 Crabtree, Pittsburgh, Pennsylvania 15261.

Project Title:
Occupational Noise Exposure, Noise-Induced Hearing Loss, and the Epidemiology of High Blood Pressure.

Principal Investigators:
Talbott, E.; Kuller, L.H.; Matthew, K., et al.

Objective:
To determine whether a group of noise-exposed individuals have elevated blood pressure independent of other known risk factors; determine if there is an increased prevalence of hypertension or an increase in mean blood pressure level in those with severe noise-induced hearing loss compared with those without such loss.

Methods or Approach:
Randomly selected male hourly workers ($n = 197$, aged 40 to 63 years) were selected from a plant near Pittsburgh, which conducts fabricating and partial assembly operations for auto parts. The mean noise level is ≥ 89 dB in the plant. The men were compared with a group of workers in an electrical heating assembly plant where the noise level was ≤ 81 dB. All subjects had worked at the plants for at least 10 years. Clinical examination included measures of height, weight, pulse, and blood pressure, and a detailed medical and personal habits history including alcohol consumption and smoking patterns. There was also a detailed questionnaire on occupational and military history and noisy hobbies. Audiometric evaluation and hearing tests were also conducted.

Results to Date:
There was no difference in mean systolic or diastolic blood pressure between workers in the two plants. However, there was a strong relationship between severe noise-induced hearing loss and high blood pressure in the >56 years age group in both plants after adjusting for risk factors ($p = 0.02$). Multiple regression techniques were used to determine which noise-related variables would best predict diastolic pressure, treated as a continuous outcome measure, while controlling for traditional risk factors for blood pressure (alcohol consumption, body mass index, age, family history of hypertension, and smoking). Noise variables entered individually into a model with blood pressure risk factors were severe noise-induced hearing loss, noisy hobbies, and military service treated as categorical variables, and noise level and duration of exposure as continuous variables. Multiple regression analysis revealed that in the noisier plant, body mass index, severe noise-induced hearing loss, and noisy hobbies explained a significant amount of the variation in diastolic pressure ($p < 0.05$), suggesting that there may be a population at increased risk for hearing loss and high blood pressure.

Future Plans:
The noise and blood pressure relationship study will be continued. Focus of new investigations will be on the hearing profile of the men with reference to speech reception and hearing performance.

Project Dates:
November 1980–November 1982.

Financial Support:
NHLBI (NIH HL-25005); EPA (CR810543-01).

1419. UNIVERSITY OF PITTSBURGH, Department of Epidemiology, 130 DeSoto Street, Pittsburgh, Pennsylvania 15261.

Project Title:
Epidemiology of Smoking Cessation and Pulmonary Function.

Principal Investigator:
Townsend, M.C.

Objective:
To validate previously observed forced expiratory volume in 1 sec (FEV_1) decrements for never smokers, ex-smokers, and current smokers with and without airways obstruction.

Methods or Approach:
Annual measurements of FEV_1, forced vital capacity (FVC), FEV_1/FVC ratio, and maximal midexpiratory flow rate (MMEF) have been made over a 6-year followup period of 645 middle-aged male participants in the Multiple Risk Factor Intervention Trial (MRFIT), Pittsburgh Center. Much attention has been paid to the quality of the spirometric testing over this period, and indices reflecting the quality of pulmonary function testing have been developed and can be used in data analysis. Cross-sectional analysis of spirometric indices by smoking status and amount smoked at baseline has been completed. Using annual lung function measurements, relative

rates of decline of spirometric indices among never smokers, ex-smokers, and continuing smokers can be examined. Since the MRFIT study is a randomized clinical trial designed to assess the effects of risk factor reduction on heart disease incidence, smoking cessation is emphasized, resulting nationally in a high proportion of ex-smokers: 47 percent of the Special Intervention group and 25 percent of the Usual Care control group smokers had quit smoking by the Fourth Annual examination. Since followup is fairly lengthy (6 years), complete (93 percent of men followed through 6 years), of good quality, and with annual spirometric testing, different FEV_1 decrements observed for never smokers, ex-smokers, and current smokers with or without airways obstruction can be validated. Analyses designed for the Pittsburgh MRFIT data are being extended to include two other MRFIT centers with good-quality measurements, increasing the sample size to 1,950 subjects.

Results to Date:
Lung function tracings are currently being measured and reviewed; no findings are available to date.

Project Dates:
May 1982–1984.

Financial Support:
NHLBI (1R23 HL28596-01).

1420. UNIVERSITY OF PITTSBURGH, Clinical Psychology Center, 4015 O'Hara Street, Pittsburgh, Pennsylvania 15260.

Project Title:
Assessment of Individual Consistency in Self-Control.

Principal Investigator:
Shiffman, S.

Objective:
To determine whether the qualities or skills associated with successful control of smoking behavior are also associated with appropriate self-management in other domains.

Methods or Approach:
Most theories of self-management attribute successful self-control to qualitites (e.g., propensity to self-reinforce) or skills (e.g., problem-solving skill) that ought to contribute to successful self-management in a variety of domains, which in turn implies that people will show a trait-like consistency in self-control. Such consistency is also implied by the ability of paper-and-pencil and laboratory assessment procedures to predict who will exercise self-control. Undergraduate psychology students (n = 400) will initially be assessed using Rosenbaum's Self-Control Schedule (SCS), a written self-report instrument. The students' self-management of a variety of problems (e.g., smoking, drinking, oral hygiene, exercise) will also be assessed by self-report. A second phase will be conducted using subjects from the upper and lower quartiles of the distribution of SCS scores. These subjects will be tested in the laboratory to determine their propensity to self-reinforce successful performances on a verbal learning task. This measure was previously related to successful smoking cessation. Finally, subjects' reports of self-control will be evaluated for consistency across problem behaviors of subjects who are consistently successful compared to those consistently unsuccessful on the written and laboratory measures.

Results to Date:
Results did not support the concept of trait-like consistency in self control. Subjects' degree of success in controlling behaviors such as smoking, overweight, and lack of exercise were not highly interrelated. Although some relationships were observed, they followed no theoretically consistent pattern. Data did not support the distinction between behaviors that need to be accelerated and those that need to be decelerated. An index of overall self control competence was moderately related to a paper and pencil measure of self reinforcement, and to the cognitive self management component of the Rosenbaum self control schedule. Laboratory data indicated that there was no relationship between laboratory measures of self-reinforcement and a paper and pencil inventory of self-reinforcement, and that the labotatory measure of self-reinforcement was unrelated to prior success in controlling smoking or overweight.

Project Dates:
January 1982–1983.

Financial Support:
University of South Florida.

1421. UNIVERSITY OF PITTSBURGH, Rehabilitation Counseling Department, 5K01 Forbes Quadrangle, Pittsburgh, Pennsylvania 15260.

Project Title:
MAPS (Maximizing Adolescent Potentials). MAPS (Minimizing Alcohol Problems and Smoking Among Youth). MAP (Minimizing Alcohol Problems By a Focus on Youth).

Principal Investigator:
Fertman, C.I.

Objective:
To design, develop, and implement primary prevention programs in schools and community settings to prevent substance use/abuse problems among youth.

Methods or Approach:
The program develops a student center in a school district that serves as a focal point for ongoing, comprehensive activities and programs concerning the prevention of tobacco, drug, and alcohol abuse problems and the promotion of healthy, responsible children and adolescents. Each program is developed to meet the needs of the district's students, faculty, and administrators. Centers are staffed by supervised prevention/intervention specialists, who have masters' degrees in psychology, counseling, or education and clinical experience in counseling and guidance of adolescents. Centers serve the general student populations and special groups at risk for developing drug and alcohol problems. Twenty-one services are available to a school district.

Results to Date:
The design, development, and implementation of a district's program are dependent on a range of factors including knowledge and attitudes of superintendents, principals, and guidance counselors and on community awareness and funding. Services are selected by principals, guidance counselors, teachers, and students. Community and parent education are essential program services.

Future Plans:
Guides will be developed for each of the 21 services offered through the center.

Project Dates:
July 1982–continuing.

Financial Support:
Allegheny County Mental Health, Mental Retardation, and Drug and Alcohol Program.

1422. UNIVERSITY OF PITTSBURGH, Victoria Building, Room 367, Pittsburgh, Pennsylvania 15261.

Project Title:
Survey of the Smoking Behaviors of Master's Prepared Clinical Nursing Specialists.

Principal Investigator:
Yasko, J.M.
Objective:
To determine the smoking histories and behaviors of master's prepared clinical nursing specialists.
Methods or Approach:
Clinical nursing specialists were surveyed by mail for past and present smoking behaviors. Areas of specialization included cardiovascular, pulmonary, oncology, and neuroscience nursing. Behaviors were assessed and demographic profiles were made for nonsmokers, previous smokers, and current smokers.
Results to Date:
Data are not yet available.
Project Dates:
February 1984–May 1985.
Financial Support:
University of Pittsburgh.

1423. UNIVERSITY OF PITTSBURGH, GRADUATE SCHOOL OF PUBLIC HEALTH, Department of Epidemiology, 127 Parran Hall, Pittsburgh, Pennsylvania 15261.

Project Title:
Followup Study of NHLBI Percutaneous Transluminal Coronary Angioplasty Registry Patients.

Principal Investigators:
Detre, K.; Kelsey, S.; Mitchell, H.
Objective:
To describe long-term mortality, morbidity, duration of angina relief, and need for subsequent revascularization among 1,800 patients who underwent a percutaneous transluminal coronary angioplasty (PTCA) procedure between 1977 and 1982; examine results in relation to baseline characteristics (including cigarette smoking) of PTCA patients.
Methods or Approach:
Contact will be maintained with 1,800 PTCA patients who were entered in the NHLBI PTCA Registry. Clinic coordinators at 18 sites throughout the United States and Canada where procedures were performed will interview patients by telephone. Data will be forwarded to the coordinating center in Pittsburgh where they will be maintained and analyzed.
Results to Date:
Of the 3,079 patients who underwent PTCA from September 1977 to 1981, who have been followed to determine natural history, approximately half remain asymptomatic, with no further procedure and no medication. Repeat PTCA and CABG was necessary in approximately 25 percent during the first year, but in very few after the first year. The death rate is approximately 1 percent/year. Thus, followup confirms the long-term efficacy of PTCA in selected patients with coronary artery disease. Although at the time of the PTCA procedure, 32 percent were cigarette smokers and 38 percent ex-smokers, there was no evidence that smokers were less likely to have a successful subsequent course.
Future Plans:
Patients will be followed through June 1987.
Project Dates:
December 1984–November 1987.
Financial Support:
NHLBI (1R01HL33292-01).

1424. UNIVERSITY OF PITTSBURGH, 647-2 Salk Hall, Pittsburgh, Pennsylvania 15261.

Project Title:
Antiviral Effect of an Acyclovir and Monoglyceride Combination on Herpes Simplex Virus.

Principal Investigators:
Fletcher, R.D.; Brastins, E.
Objective:
To determine if combination treatment (acyclovir and monoglycerides) can prevent development of viral resistance to acyclovir; ascertain if *Herpes simplex* virus (HSV) isolates from smokers and nonsmokers have the same ability to develop resistance to acyclovir.
Methods or Approach:
HSVs, isolated from hospital or clinic patients, are replicated in epithelial-like gingival cells. The viral titers following treatment with acyclovir, monolaurin, or a combination were measured by microtiter techniques. Percent inhibition was calculated from $TCID_{50}$ titers. Viability on subcultures was detected in untreated cell systems.
Results to Date:
Combinations of acyclovir and monolaurin demonstrated enhanced inhibition of HSV-2 (MS) compared with either chemical tested separately. Gingival cells treated with the combination showed no viral damage microscopically. The combination of 0.24 and 0.48 μg/mL acyclovir and 18 μg/mL monolaurin resulted in the loss of HSV-2 viability.
Future Plans:
Future plans include evaluation of HSVs isolated from smokers and nonsmokers for resistance to acyclovir. Also, the antiviral effect of the combination (acyclovir and monoglycerides) on these isolates will be determined.
Project Dates:
June 1983–1988.
Financial Support:
University of Pittsburgh.

1425. UNIVERSITY OF PITTSBURGH, Department of Epidemiology, Graduate School of Public Health, 130 DeSoto Street, Pittsburgh, Pennsylvania 15261.

Project Title:
Seven Year Mortality From Cancer and CHD – A Followup Linking Screening Data on Occupation and Risk Factors From Two Sources.

Principal Investigators:
Meilahn, E.N.; Kuller, L.H.
Objective:
To (1) characterize occupations by risk factor prevalence; (2) determine race-specific mortality rates from cancer with particular emphasis on cancer of the lung; and (3) compare all-cause and cause-specific mortality rates by job classification, controlling for selected demographic and health factors.
Methods or Approach:
Variation in mortality by occupation has been linked to worksite exposures. Few studies, however, have been able to assess the effect of individual risk factors on differential mortality rates among workers. A combination of two large data sets allowed analysis of individual risk factor levels by job category. In 1974-1975, the Multiple Risk Factor Intervention Trial (MRFIT) screened workers in Allegheny County, Pennsylvania, for serum cholesterol, cigarettes/day, diastolic blood pressure, history of diabetes and heart attack, age, and race. Long-term job history (1930 to 1970) in steel plants, compiled for the Allegheny County Steelworkers Study (SWS), was

available for 3,995 of the MRFIT ineligible screenees. Risk factor levels of men in job categories exhibiting excess mortality in the SWS, such as coke plant workers, were compared with those from the remainder of the cohort. In addition, ascertainment of vital status and cause of death were determined for MRFIT nonrandomized screenees through June 1981. Initial descriptive analyses revealed risk factor variation by job classification.

Results to Date:

Preliminary findings show that fewer coke plant workers smoked than other workers and black coke plant workers who smoked consumed fewer cigarettes/day than white workers. White-collar workers had nonsignificantly higher levels of smoking and cholesterol than coke plant workers and higher diastolic blood pressure, despite a larger proportion of blacks (26.6 percent) found in the coke plant compared with white-collar workers (1.0 percent). Other high-risk work areas to be assessed include open hearth, foundry, mason department, billet, bloom and slab mills, and blast furnace. Mortality results have not yet been analyzed.

Project Dates:

August 1984–August 1985.

Financial Support:

University of Pittsburgh.

1426. VETERANS ADMINISTRATION MEDICAL CENTER, 178 Pinewood Drive, Bridgeville, Pennsylvania 15017.

Project Title:

Effectiveness of Short Term Smoking Cessation Behaviors of Patients and Hospital Employees.

Principal Investigators:

Meyer, C.D.; Bohachick, P.A.

Objective:

To examine the effects of two types of smoking cessation/reduction programs on smoking behavior of patients and employees of an acute care health facility compared with a control group; study the relationship between smoking behavior and selected background variables (gender, pack years of smoking, and type of smoking as determined by Horn's Smoker's Self Test).

Methods or Approach:

Cigarette smokers were randomly assigned to a (1) therapist conducted (TC), self-administered (SA), or control group. Participants in the experimental groups had individual carbon monoxide (CO) analysis and selected spirometry tests, and completed a consent form, Horn's "Why Do You Smoke" questionnaire, and a pretest smoking intake assessment. Each received a detailed explanation of the computerized spirometry printout graph and on the effects of CO on the body. They also received a packet of smoking literature and were instructed to read it. The TC group attended a 2-hour group meeting at which different quitting strategies were discussed. The SA group was told that they were to try to quit on their own and would be contacted. The TC and SA groups were contacted 2 weeks later to complete the posttest questionnaire.

Results to Date:

ANOVA indicated that both experimental groups showed significant reductions in smoking compared with the control group, but the Scheffe procedure suggested that neither treatment was significantly more effective than the other; however, raw data indicate that the treatment groups had different types of reduction. Mean percentage of cigarette reduction in the TC group (46.89 percent) was greater than in the SA group (34.95 percent). The TC group had the greatest overall percentage of cigarette reduction for the total number of smoked cigarettes, but the SA group had more people reducing the number of cigarettes smoked. Also, there was no relationship between smoking type and reduction. Contrary to previous reports, women were more successful than men in reducing smoking (p, 0.05). There were no significant differences between blacks and whites in cigarette reduction. Results of 6-month followup (percentages of those reached rather than of the original groups) showed that 71 percent of TC and 57 percent of SA were smoking less than at the beginning of the study compared with 27 percent of controls.

Future Plans:

A pilot program consisting of smoking cessation classes will be offered to patients, families, and employees on a patient unit.

Project Dates:

September 1984–June 1985.

Financial Support:

VA.

1427. VETERANS ADMINISTRATION MEDICAL CENTER, Black Horse Road, Coatesville, Pennsylvania 19320.

Project Title:

Experimental Investigation of the Components of Smoking Behavior.

Principal Investigator:

Ainslie, G.W.

Objective:

To precisely time smokers' preferred puffing movements in a naturalistic setting; see how preference for various puff lengths is affected by delay from moment of choice.

Methods or Approach:

An Apple microprocessor with a specially designed input/output interface is used to control a cigarette holder with a polyethylene side tube (which can measure and/or control the length of cigarette puffs) while hospitalized alcoholic subjects pursued normal activities in the dayroom. Arrangements have been made with the staff of a 10-bed alcohol rehabilitation unit, where patients are restricted from smoking for a 12-hour period three times a week, to study the motive to smoke at the end of restricted periods. This ward has a terminal connected to a DEC PDP 11/24 minicomputer with a MUMPS running system. Self-report measures of reasons for smoking and various ego functions are being programmed for automated administration.

Results to Date:

Results are not yet available.

Financial Support:

VA.

1428. VETERANS ADMINISTRATION, 1076-B Wayne Avenue, Coatesville, Pennsylvania 19320.

Project Title:

Protection Against Toxicants of Alcoholism and Smoking: Rat Studies.

Principal Investigator:

Sprince, H.

Objective:

To screen certain sulfur compounds and certain naturally occurring metabolites (e.g., L-cysteine, thiamin, L-ascorbic acid) for protective action in rats against lethality of acetaldehyde (AcH), acrolein (AcrH), and formaldehyde (FmH) in a search for effective protectants against these aldehydes and aldehydes in general

Methods or Approach:
Male rats ($\geq$ 10/group) of a given strain, age, and weight were fasted overnight and pretreated orally or i.p. with protectant being tested. Thirty minutes later, the test toxicant was administered orally at LD 90 dose level. Control rats were pretreated with saline before treatment with test toxicant. Rats were observed over a 72-hour period for adverse and lethal effects.
Results to Date:
Good protection (approximately $\geq$80 percent survivors) against AcH was obtained with L-cysteine (C), N-acetylcysteine (NAC), thiamin hydrochloride (T), Na metabisulfite, L-cysteic acid, and L-ascorbic acid (A). NAC gave 100 percent protection, as did a combination of CTA. Both C and A also protected well against AcrH, but were less effective against FmH. However, repeated pretreatment with A alone against FmH resulted in 90 percent survivors. Protection of sulfur compounds and L-ascorbic acid against the aldehyde toxicants suggest potential for beneficial effects in alcoholism and smoking; however, further research is necessary.
Financial Support:
VA.
Reference:
Sprince, H. *Protective Action of Sulfur Compounds Against Aldehyde Toxicants in Cigarette Smoke* (In press).

Rhode Island

1429. BIOSPEC, INC., 147 Sixth Street, Providence, Rhode Island 02906.

Project Title:
Polymer Fume Fever and Smoking.

Principal Investigator:
Donnelly, G.M.
Objective:
To study the relationship between smoking and polymer fume fever.
Methods or Approach:
Workplaces that use polytetrafluoroethylene (PTFE) and have the potential for incidents of polymer fume fever will be studied; conditions that have resulted in incidents will be reviewed; and smoking habits of individuals who have experienced polymer fume fever will be surveyed. Other factors to be assessed include company smoking policy, time lost from work, frequency of polymer fume fever in the candidate work force, and frequency of fever in smokers vs. nonsmokers.
Results to Date:
Cooperating employers are being identified.
Project Dates:
November 1984–May 1986.
Financial Support:
BIOSPEC, Inc.

1430. BROWN UNIVERSITY, MEMORIAL HOSPITAL, Prospect Street, Pawtucket, Rhode Island 02860.

Project Title:
Pawtucket Heart Health Program.

Principal Investigators:
Carleton, R.A.; Lasater, T.M.
Objective:
To test the hypothesis that community-wide multifaceted educational processes (targeted at low levels of physical fitness, smoking, hypercholesteremia, high blood pressure, and obesity) will change population lifestyle, population risk factors, and ultimately, cardiovascular mortality and morbidity.
Methods or Approach:
In both the education city and the comparison city, baseline and followup risk factor surveys assessing knowledge, attitudes, behavior, and physiologic risk factors will be conducted. Ongoing mortality and morbidity surveillance will permit estimation of changes in myocardial infarction and stroke rates and deaths. In the education city, a multifaceted intervention targeting individuals, groups, entire organizations, and the entire community is presently being implemented. The intervention is based on social learning theory, behavior community technology, and other scientific disciplines to achieve a process of community activation for health promotion.
Results to Date:
Two initial risk factor surveys have been completed. Change is occurring in this high-risk city.
Future Plans:
It is anticipated that community ownership will occur during the evolution of this project, and the health promotion/disease prevention activities will continue beyond the funded duration of the project.
Project Dates:
August 1980–1986.
Financial Support:
NHLBI (HL 2[illegible]629).

1431. BROWN UNIVERSITY, MIRIAM HOSPITAL, Division of Behavioral Medicine, 164 Summit Avenue, Providence, Rhode Island 02906.

Project Title:
Self-Help Smoking Cessation for Women at the Worksite.

Principal Investigators:
Abrams, D.B.; Follick, M.J.
Objective:
To provide a controlled evaluation of short and long-term effectiveness of self-help smoking cessation programs in a worksite setting.
Methods or Approach:
The 5-year program will be conducted in two parts. Study 1 is a controlled, randomized trial that compares an individually-administered self-help protocol, a group-administered self-help protocol, and a minimal treatment control. Three worksites will increase sample size ($n = 540$) and generalizability and multiple measures of outcome will be used. Subjects will be followed for 12 months. Smoking outcomes, including cessation and reduction rates, will be measured using self-report, saliva cotinine, and corroboration from a significant other. Mediating mechanisms will be examined including measures of social support. Results will provide a test of self-help worksite programs and will show which of the two formats employed is the most effective. Study 2 will determine if efficacy of the optimal self-help program is significantly enhanced by addition of an "organizational" component designed to maximize the unique worksite resources. The organizational component

includes media feedback, competition, and other social influence procedures. Of the four matched worksites involved, two will be randomly assigned to the self-help plus organization component condition and two to the self-help alone condition. Participants will be evaluated on similar measures and at the same times as in study 1. A combined cross-sectional and cohort telephone survey will also be employed to evaluate the diffusion effects of the interventions on all smokers, including nonparticipants. Cost effectiveness will be used to evaluate final outcomes. Results of both studies should yield sufficient information to identify an optimal worksite-based, replicable, and relatively inexpensive self-help smoking cessation program.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Findings will be used to develop a comprehensive treatment model for cost effective worksite smoking cessation, which will be tested in multiple worksites of different sizes and types.

Project Dates:
September 1984–September 1989.

Financial Support:
Brown University, Miriam Hospital; NCI (CA 31389).

1432. BROWN UNIVERSITY, MIRIAM HOSPITAL, Division of Behavioral Medicine, 164 Summit Avenue, Providence, Rhode Island 02906.

Project Title:
Psychosocial Stressors, Smoking Cessation and Coronary Heart Disease at the Worksite.

Principal Investigators:
Abrams, D.B.; Monti, P.M.

Objective:
To explore the relationship between (1) individual differences in psychosocial stress and social support variables relevant to smoking; (2) three promising treatments for relapse prevention and maintenance of nonsmoking; (3) intermediate outcome in terms of changes in coping responses (cognitive, behavioral, and psychophysiological arousal regulation); and (4) treatment outcome (or associated relapse process).

Methods or Approach:
Comprehensive evaluation of the feasibility of implementing behavioral smoking cessation at the worksite will be conducted on male and female smokers, to examine the individual difference dimension and its interaction with treatment outcome. At replications (36 subjects in each) undertaken in three worksites, participants will receive a nicotine-fading behavioral cessation protocol and will be assigned to either (1) standard maintenance (contact time and health education); (2) cognitive-behavioral stress management; or (3) social skills social network support for relapse prevention. A comprehensive behavioral assessment battery, administered pre- and posttreatment, will evaluate skill acquisition (with continuous monitoring of psychophysiological arousal) in analogue stress situations and assess cognitive, behavioral, and social coping skills; social supports; and self-efficacy expectations. At followup, a comprehensive relapse interview with the client and a significant other in the social network will be conducted. Self-report measures of smoking status will be corroborated by collateral informants and breath samples of carbon monoxide. Participants will be followed for 12 months.

Results to Date:
Preliminary results reveal that selected psychosocial stress variables discriminate successful quitters from relapsers on the assessment battery. Relapsers have higher psychophysiological reactivity to laboratory stressors; higher self-reported anxiety; and lower coping skills in response to negative emotional states. However, relapsers do not differ from quitters in general social skills, social anxiety, or social support, suggesting that intrapersonal stress reactivity rather than social factors is related to relapse. Relapsers were more reactive to social situations involving the sight and smell of cigarettes; smoking cues in conjunction with social situations may be powerful triggers of relapse. High nicotine dependent smokers were significantly less successful and were less able to quit smoking on quit day. Social skills and social support training was not well received despite its intuitive appeal in a worksite setting. Followup is still in progress.

Future Plans:
Specific components will be developed, tailored to the needs of smokers at the worksite. Personal stress and high nicotine dependence are two dimensions that might make it more difficult for smokers to quit.

Project Dates:
September 1983–September 1985.

Financial Support:
Brown University, Miriam Hospital; NHLBI (5R01HL32318).

1433. ROGER WILLIAMS GENERAL HOSPITAL, BROWN UNIVERSITY PROGRAM IN MEDICINE, 825 Chalkstone Avenue, Providence, Rhode Island 02908.

Project Title:
The Effects of Renal Function on Nicotine Metabolism.

Principal Investigators:
Trebbin, W.M.; Perry, R.J.

Objective:
To study nicotine and cotinine levels in smoking and nonsmoking subjects (with varying degrees of renal failure but not requiring dialysis) after smoking a standard cigarette; compare results with levels in controls with normal renal function.

Methods or Approach:
Nicotine and its metabolites are excreted almost exclusively in the urine. Higher serum nicotine levels have been found in a hemodialysis population, and it is hoped that results will provide a better understanding of nicotine pharmacodynamics in patients with varying degrees of impaired excretion of nicotine. Subjects and controls will be divided into smokers and nonsmokers, matched for age and sex. Patients will be further stratified according to levels of renal function determined by creatinine clearance. Candidates with liver disease will be excluded, and all subjects will have liver function tests prior to participation. After periods of abstention, subjects will be exposed to standard cigarettes containing known amounts of nicotine, and nicotine and cotinine levels will be surveyed at fixed intervals following exposure. Physiologic parameters will also be followed. Clinical testing will take place in a smoke-free environment.

Results to Date:
Comparison of patients with end stage renal disease (on maintenance dialysis) and controls with normal renal function showed that nicotine levels were significantly higher in patients. Data on patients on continuous ambulatory peritoneal dialysis are not yet available.

Future Plans:
Under consideration are studies on the effect of sex differences in nicotine handling, effects of nicotine on renal prostaglandins, kinins, and other vasoactive substances, and passive smoking data.

Project Dates:
July 1982–May 1985.
Financial Support:
CTR.
Reference:
Perry, R.J.; Trebbin, W.M. "Elevated Nicotine Levels in Patients Undergoing Hemodialysis. A Role in Cardiovascular Mortality and Morbidity?" *American Journal of Medicine* 76:241-246, February 1984.

1434. UNIVERSITY OF RHODE ISLAND, Kingston, Rhode Island 02881.

Project Title:
Informal Self-Help Approaches to Smoking Cessation.

Principal Investigator:
Prochaska, J.O.
Objective:
To determine the processes used by self-quitters to enter the revolving door of change, to move through each stage of the process, and to exit into a nonsmoking lifestyle.
Methods or Approach:
Study subjects (n = 1,000) were recruited representing five key stages of change: precontemplation, contemplation, action, maintenance, and relapse. Subjects completed an extensive retrospective and current questionnaire, an interview, and a saliva test for smoking status. Analyses of the change processes section of the questionnaire are extremely encouraging, since the factor structure is very consistent with the revolving door model of change. Specifically, the 40-item test yields 10 highly reliable and strongly defined scales for measuring the following distinct processes of change: (1) consciousness raising, (2) self-reevaluation, (3) environmental reevaluation, (4) self-liberation, (5) social liberation, (6) counterconditioning, (7) stimulus control, (8) contingent reinforcement, (9) dramatic relief, and (10) helping relationship.
Results to Date:
Data indicate that, as predicted, there are highly significant relationships between the stage of change subjects are in and the processes of change used most. Specifically, smokers in the precontemplation stage use denial and active avoidance to resist any internal pressure to change. Contemplators emphasize consciousness raising and self-reevaluation, with self-reevaluation procedures appearing to be the process that allows for the transition from contemplation into action. Recent quitters in the action stage use the most processes with self-reevaluation, self-liberation, contingent reinforcement, counterconditioning, and stimulus control being emphasized. The maintenance group appears to emphasize counterconditioning and stimulus control procedures, although they also have the benefit of having succeeded in earlier stages of change. Relapsers appear to revolve back into contemplation. Six significant discriminative functions have been developed for predicting movement for the groups representing the precontemplation, contemplation, action, and relapse stages. Functions were able to predict who would progress, who would regress, and who would stay the same from initial assessment to first 6-month followup. Variables entered with the discriminative functions included the 10 processes of change, 2 decisionmaking measures, self-efficacy, and temptation levels in different smoking situations. Another 17 predictors, including smoking history, health history, demographics, stress, and withdrawal symptoms, were not nearly as effective as predictors of change in smoking attitudes and behaviors. Subjects were followed every 6 months for 2 years. Profile analyses identified different patterns of change over time. Processes of change, self-efficacy, and decisional balance variables were clearly related to longitudinal changes in stages of smoking cessation. Data and models of self-change generated are being used to develop more effective self-help materials for smoking cessation.
Project Dates:
May 1980–April 1983.
Financial Support:
NCI (CA 27821).
References:
(1) DiClemente, C.C. "Self-Efficacy and Smoking Cessation Maintenance." *Cognitive Therapy and Research* 5:175-187, 1981. (2) DiClemente, C.C.; Prochaska, J.O. "Self-Change and Therapy Change of Smoking Behavior: A Comparison of Processes of Change in Cessation and Maintenance." *Addictive Behaviors* 7:133-142, 1982. (3) Prochaska, J.O.; Crimi, P.; Lapsanski, D., et al. "Self-Change Processes, Self-Efficacy and Self Concept in Relapse and Maintenance of Smoking Cessation." *Psychological Reports* 51(1):983-990, December 1982. (4) Prochaska, J.O.; DiClemente, C.C. "Stages and Processes of Self-Change in Smoking: Toward an Integrative Model of Change." *Journal of Consulting and Clinical Psychology* 51(3):390-395, June 1983. (5) Prochaska, J.O.; DiClemente, C.C. "Self Change Processes Self Efficacy and Decisional Balance Across Five Stages of Smoking Cessation." In: *Advances in Cancer Control – 1983.* New York, Alan R. Liss, Inc., 1984, pp. 131-140. (6) Velicer, W.; DiClemente, C.C.; Prochaska, J., et al. "A Decisional Balance Measure for Predicting Smoking Cessation." *Journal of Personality and Social Psychology* (In press).

1435. UNIVERSITY OF RHODE ISLAND, Kingston, Rhode Island 02881.

Project Title:
Self-Help Models and Manuals for Smoking Cessation.

Principal Investigator:
Prochaska, J.O.
Objective:
To develop and disseminate more effective models and manuals for individuals wishing to quit smoking on their own.
Methods or Approach:
The study is a continuation of 3 years of research on self-change approaches to smoking cessation, which enhanced a Transtheoretical Model that involves 10 change processes receiving differential use during four stages of change: precontemplation, contemplation, action, and maintenance. Causal modeling will be applied to a 2-year longitudinal data set of 950 smokers and former smokers. Structural analyses will test causal models of change processes that determine progress between each stage of change. Three competing theories are being tested: (1) self-efficacy; (2) decisionmaking; and (3) cognitive-behavioral theory of relapse. Profile analyses will assess patterns of change demonstrated during the 2-year period of quitting smoking. Causal models and profile analyses are being used to develop self-help manuals for smokers at four different stages of change.
Results to Date:
To date, the following self-help programs have been developed: (1) self-administered manual for people in the action stage; (2) therapist-administered manual for people in the action stage; (3) self-administered manual for people in the contemplation stage; (4) computer-assisted correspondence course for the contemplation stage; (5) computer-assisted correspondence course for the action step; and (6) second generation self-administered action manual. The self-administered and thera-

pist-administered action manuals were compared with the American Lung Association's self-help manual. All manuals demonstrated remarkable delayed action effects, with more participants taking action at 6-month followup than at 1-month followup. However, in both the self-administered and therapist-administered conditions, the transtheoretical programs outperformed the ALA manual; two to three times as many participants took action and maintained action at 6-month followup than participants in the ALA program. Results of initial studies offer encouragement for developing more effective self-help programs based on self-change data and models of smoking cessation.

Financial Support:
NCI (CA 27824).

References:
(1) DiClemente, C.C.; Prochaska, J.O. "Processes and Stages of Change: Coping and Competence in Addictive Behavior Change." In: Shiffman, S.; Wills, T. (Editors). *Coping and Substance Abuse.* New York, Academic Press (In press). (2) Prochaska, J.O.; DiClemente, C.C. *The Transtheoretical Approach.* Homewood, Illinois, Dow Jones/Irwin, Inc., 1984. (3) Prochaska, J.O.; DiClemente, C.C. "Common Processes of Change for Psychological Distress, Overeating, and Smoking Cessation." In: Shiffman, S.; Wills, T. (Editors). *Coping and Substance Abuse.* New York, Academic Press (In press).

1436. VETERANS ADMINISTRATION MEDICAL CENTER, 380 Westminster Mall, Providence, Rhode Island 02903.

Project Title:
Smoking Cessation in Pulmonary Patients.

Principal Investigators:
Sirota, A.D.; Curran, J.P.; Panciera, T., et al.

Objective:
To examine the effectiveness of a smoking cessation program for VA outpatients with chronic pulmonary disease.

Methods or Approach:
Treatment, administered during nine weekly 1-hour group sessions, consists of a comprehensive approach including gradual nicotine withdrawal, self-management strategies, and relapse prevention techniques. Measures include self-monitoring of number of cigarettes smoked and daily nicotine intake, weekly measures of carbon monoxide (CO) in expired air, pretests and followup pulmonary function tests, and pretreatment, posttreatment, and followup serum thiocyanate levels.

Results to Date:
Approximately 60 patients have completed treatment and about 50 percent have succeeded in quitting smoking, some on 1-year followup. CO and serum thiocyanate measures corroborate self-report. Preliminary results suggest that a population of chronically ill men can benefit from a multimodal smoking cessation program.

Financial Support:
VA.

1437. VETERANS ADMINISTRATION, Davis Park, Providence, Rhode Island 02908.

Project Title:
The Dialyzability of Nicotine.

Principal Investigators:
Trebbin, W.M.; Solomon, R.

Objective:
To determine if nicotine is dialyzable.

Methods or Approach:
Hemodialysis patients will be placed in a relatively smoke-free environment and 15 ml of blood will be drawn as a baseline. Next, a standard cigarette will be smoked and a second 15 ml of blood will be drawn. All blood will be analyzed for blood urea nitrogen, creatinine, and nicotine levels. At another institution, healthy nondialysis volunteers will be kept in a relatively smoke-free environment, offered the same timed specimens, consume the same standard cigarette, but will not be dialyzed. This population will constitute a control population. All results will be subjected to statistical analysis.

Results to Date:
This project is now underway and data are being collected.

Financial Support:
VA.

1438. VETERANS ADMINISTRATION, Davis Park, Providence, Rhode Island 02908.

Project Title:
Renal Failure and Nicotine.

Principal Investigators:
Trebbin, W.M.; Perry, R.J.

Objective:
To assess nicotine levels in patients with varying degrees of renal failure; compare this to controls with normal renal function.

Methods or Approach:
Blood will be assayed for nicotine in samples obtained from smokers and nonsmokers (but not former habitual smokers) after a nicotine-free interval of at least 12 hours. A sample will be obtained prior to smoking a standard cigarette, 2 minutes after completion of the cigarette, and 30 and 60 minutes after the completion of the cigarette. Patients will remain in a smoke-free environment for the duration of the protocol. Prior to smoking the test cigarette, blood will be obtained for determination of blood urea nitrogen, creatinine, hematocrit, serum glutamic oxaloacetic transaminase, lactate dehydrogenase, bilirubin, and alkaline phosphatase. Risks are minimal and confined to those associated with venipuncture and the changes in blood pressure and pulse associated with the smoking of a single cigarette. Total amount of blood required will be 28 ml per subject.

Results to Date:
Project is in a preliminary phase.

Financial Support:
VA.

1439. VETERANS ADMINISTRATION, Davis Park, Providence, Rhode Island 02908.

Project Title:
Assessment of the Effects of Cigarette Smoking on Subjective and Physiological Sexual Arousal in a Healthy Female Population.

Principal Investigators:
Wincze, J.P.; Balko, A.; Sirota, A.D., et al.

Objective:
To determine the effects of cigarette smoking on vaginal vasculature in a healthy female population; determine whether physiological and/or subjective sexual arousal in response to videotaped erotic stimuli is affected by cigarette smoking.

Methods or Approach:
Ten volunteers from Brown University who are smokers will be assigned to one of two groups in a multiple baseline. Patients will view a brief sexually arousing videotape (VT)

followed by smoking a cigarette, followed by a second VT (group BA); or view one VT, have a 10-min rest period, view a second VT, smoke a cigarette, and then view a third VT (Group ABB). Sexual and smoking histories will be determined before the experiment. Physiological and subjective measures of arousal as well as carbon monoxide levels will be determined at appropriate intervals before, during, and following the VTs.
Results to Date:
Project is in a preliminary phase.
Project Dates:
March 1984–continuing.
Financial Support:
VA.

1440. VETERANS ADMINISTRATION, Davis Park, Providence, Rhode Island 02908.

Project Title:
Assessment of the Effects of Cigarette Smoking on Subjective and Physiological Sexual Arousal in Persons With Vascular Disease.

Principal Investigators:
Wincze, J.P.; Sirota, A.D.; Balko, A.B., et al.
Objective:
To determine the effects of cigarette smoking on penile vascular changes in patients with known vascular disease; determine whether physiological and/or subjective sexual arousal in response to videotaped erotic stimuli is affected by cigarette smoking in these patients.
Methods or Approach:
Ten volunteers from inpatient surgical services who are smokers and who demonstrate attenuated erectile responsivity will serve as subjects. Patients will be assigned to one of two groups in a multiple baseline design. Patients will view a brief sexually arousing videotape (VT) followed by smoking a cigarette, followed by a second VT (Group BA); or view one VT, have a 10-minute rest period, view a second VT, smoke a cigarette, and then view a third VT (Group BAA). Sexual and smoking histories will be determined before the experiment. Physiological and subjective measures of arousal as well as carbon monoxide levels will be determined at appropriate intervals before, during, and following the VTs.
Results to Date:
Project is in a preliminary phase.
Financial Support:
VA.

1441. VETERANS ADMINISTRATION, Davis Park, Providence, Rhode Island 02908.

Project Title:
Evaluation of the Impact of Behavioral Risk Factors on Medical Utilization.

Principal Investigators:
Curran, J.P.; Sirota, A.
Objective:
To (1) discover the prevalence of smoking and obesity in the Providence Veterans Administration Medical Center inpatient population; (2) discover the relationship between these factors and the degree and type of medical services utilized by the patients; and (3) identify a group of people whose smoking and eating behavior puts them at significant medical risk, thus setting the stage for developing treatment programs that will modify these behaviors.
Methods or Approach:
Relevant data will be collected from a retrospective survey of medical charts and from a questionnaire mailed out to each of the patients in the sample.
Results to Date:
Project is in a preliminary phase.
Financial Support:
VA.

South Carolina

1442. CLEMSON UNIVERSITY, Department of Management, Clemson, South Carolina 29631.

Project Title:
Health Evaluation Project of the OCHAMPUS Employee Health Promotion Program.

Principal Investigator:
Hendrix, W.H.
Objective:
To establish individual, organizational, and extra-organizational factors predictive of stress, coronary artery disease risk, and organizational performance; evaluate effectiveness of interventions to improve health, including exercise and stress management.
Methods or Approach:
Evaluation of health interventions to be established by a pretest–posttest control group design using analysis of covariance. Causal paths leading from individual, organizational, and extra-organizational factors to stress, coronary artery disease risk, and organizational effectiveness will be established using path analysis.
Results to Date:
Job and life stress were related to an increase in absenteeism, a decrease in performance, and number of cold/flu episodes/year. Risk of coronary artery disease, measured by the ratio of total serum cholesterol divided by high density lipoprotein cholesterol, was found to increase in sedentary, overweight males who smoked cigarettes. Job stress tended to decrease job satisfaction and organizational commitment and increase somatic symptoms (e.g., headache and fatigue).
Project Dates:
March 1983–January 1985.
Financial Support:
DOD, Office of Civilian Health and Medical Program of the Uniformed Services (MDA 90683-m-0046).

1443. UNIVERSITY OF GEORGIA, SAVANNAH RIVER ECOLOGY LABORATORY, P.O. Drawer E, Aiken, South Carolina 29801. E.I. DU PONT DE NEMOURS AND CO., SAVANAH RIVER LABORATORY, Aiken, South Carolina 29808.

Project Title:
Contribution of a Nuclear Fuel Chemical Separations Facility to the Plutonium Content of a Tobacco Crop.

Principal Investigators:
McLeod, K.W.; Pinder, J.E., III.; Watts, J.R.

Objective:
To evaluate the potential dose-to-man from interception and retention of plutonium (Pu) from tobacco grown near a chemical separations facility at the Savannah River Plant (SRP) that releases Pu to the atmosphere.
Methods or Approach:
A tobacco crop was grown in a field 420 m northwest of an emission stack at the separations facility. A sample of the seedlings planted was taken to measure Pu content. The crop was raised according to common tobacco farming techniques and yielded an early (July) and late (September) harvest. Stems were sampled at the end of the season.
Results to Date:
Average leaf ^{238}Pu and ^{239,240}Pu concentrations were 9.8 and 5.1 fCi/g dry weight, respectively, indicating that 2.5 percent of the deposition occurring during the tobacco growth period was on merchantable leaves. Leaf Pu concentrations were slightly greater than Pu concentration of stem tissue. Tobacco grown near the facility had 10 times higher Pu concentrations than that grown off the SRP. Pu concentrations were similar to other broadleaf crops; however, since the inhalation pathway contributes more to Pu dose than the ingestion pathway, dose commitment would be 1,000 times greater for tobacco usage than wheat or soybean consumption when crops were grown under identical Pu deposition situations.
Financial Support:
DOE (EY76C090819); E.I. du Pont de Nemours and Co. (AT(07-2)-1).
Reference:
McLeod, K.W.; Pinder, J.E., III; Watts, J.R. "Contribution of a Nuclear Fuel Chemical Separations Facility to the Plutonium Content of a Tobacco Crop." *Health Physics* 46(6):1205–1211, 1984.

1444. USDA, ARS, CLEMSON UNIVERSITY, Clemson, South Carolina 29631.

Project Title:
Nutrient Status and Hypertension in South Carolina Adolescents.
Principal Investigator:
Borgman, R.F.
Objective:
To determine etiology of hypertension in South Carolina adolescents with special emphasis on nutrient intake.
Methods or Approach:
Adolescents attending 4-H camps in South Carolina will be questioned about dietary habits, general dietary likes and dislikes, county of residence, and exercise patterns. Blood pressures of subjects and matched controls will be determined, and taste acuities for sucrose, sodium chloride, urea, and hydrochloric acid will be determined. Hair samples will be taken and analyzed for Zn, Cd, Cu, Cr, Se, and Pb. Blood pressures will be correlated with these factors, as will race and sex.
Results to Date:
Studies with over 750 university students revealed approximately 10 percent to be hypertensive (pressures over 159 systolic and/or 89 diastolic). Positive correlations between blood pressures were found with age, height, weight/height, and alcoholic beverage consumption. In some studies, students stating a preference for salty foods had higher pressures. No association was noted between blood pressures and psychological profile, taste acuity, or tobacco usage. Hair and saliva concentrations of sodium, potassium, calcium, and magnesium were sometimes correlated with blood pressure, but the degree of association was not sufficient to be useful clinically. Hair lead concentrations were often positively correlated with blood pressure. Intervention and prevention techniques for hypertension in university students appear to be (1) maintain an ideal body weight, (2) avoid excessive salt intake, and (3) limit consumption of alcoholic beverages.
Project Dates:
July 1980–December 1983.
Financial Support:
USDA (SC00425).

Tennessee

1445. CARTER-UNICOI-JOHNSON HEALTH DISTRICTS, Carter County Health Department, P.O.Box 788, Elizabethton, Tennessee 37643.

Project Title:
Health Education Risk Reduction Project. Antismoking/Smoking Prevention.
Principal Investigators:
Henson, T.H.; Verble, S.D.
Objective:
To (1) increase group knowledge of the risks and effects involved in cigarette smoking; (2) increase the awareness of the importance of establishing good health habits early in life; and (3) provide voluntary smoking cessation clinics for interested adults in Carter and Unicoi counties.
Methods or Approach:
The project (1) evaluated and identified all existing resources and current services aimed at adolescent tobacco use; (2) established an advisory committee; (3) developed and implemented a risk assessment survey to solicit information regarding adolescent behavior related to smoking and tobacco use; (4) developed a teaching unit for adolescents focusing on the direct effects of smoking; (5) coordinated with local school systems for the implementation of the unit (target group, fifth grade); (6) conducted a followup health risk assessment at end of school year; (7) identified available smoking cessation programs and selected American Lung Association's "Freedom From Smoking"; and (8) promoted and conducted smoking cessation clinics within the communities. A health risk assessment survey and pre- and posttest knowledge test were administered to students to determine level of comprehension of teaching unit. Students and teachers made subjective evaluations on performance of health educators and materials presented. A time–trend study is being conducted.
Results to Date:
Final results are not yet available.
Future Plans:
Teacher training is planned so that the education program will be ongoing; program will be expanded to include other health risks (alcohol and drugs, exercise, nutrition, stress, safety).

Project Dates:
March 1981–June 1985.
Financial Support:
Carter County Government (110-44171-440).

1446. EAST TENNESSEE STATE UNIVERSITY, COLLEGE OF MEDICINE, Department of Surgery, Johnson City, Tennessee 37614.

Project Title:
Chronic Tobacco Smoke Exposure in Primates.

Principal Investigators:
Bryant, L.R.; DeLucia, A.J.
Objective:
To develop and test a subhuman primate model to study chronic effects of cigarette smoke.
Methods or Approach:
Male stumptailed macaques (*Macaca Arctoides*) were selected as the experimental animal to simulate smoking in humans. All animals were fed a high-fat diet (45 percent of calories from fat, average total plasma cholesterol 400 mg/dL). Animals were exposed to whole cigarette smoke through custom-fitted facemasks while seated in an aluminum smoking chair. Use of one-way inhalation valves allowed measurement of total particulate matter (TPM) uptake by each monkey. High-dose animals (two exposure sessions/day) and low-dose animals (one exposure session/day) retained approximately 35 to 40 mg of total particulate matter/session. All animals were killed after 50 to 94 months of exposure. The following tests were performed prior to necropsy: (1) multiple- and single-breath N_2 washout; (2) lung macrophage (PAM) glutathione and antioxidant enzymes; (3) PAM superoxide production and chemiluminescence during particle phagocytosis; (4) platelet function; (5) mitogenic response of peripheral lymphocytes; (6) 2,3 diphosphoglycerate (6) plasma cholesterol and triglycerides; (7) serum and lung lavage proteinase-inhibitor activity; (8) plasma levels of vitamins E, A, and C; (9) plasma cortisol levels; (10) phospholipid fatty acid profiles of PAMs and blood cells; and (11) blood carboxyhemoglobin, nicotine, and cotinine levels after smoking. At necropsy, tissues were obtained for chemical and microscopic evaluation of vascular lesions, a complete endocrine examination, light- and electron-microscopic lung examination, and measurement of antioxidant and biotransformation enzymes of lung and other tissues, and splenic lymphocyte natural killer cell activity.
Results to Date:
Results from some studies have not been fully analyzed. Significant differences between smokers and controls were found for (1) PAM and lung glutathione and antioxidant levels; (2) mitogenic response of splenic and peripheral lymphocytes; (3) diminished natural killer cell activity of splenic lymphocytes; (4) decreased erythrocyte 2,3 disphosphoglycerate levels; and (5) decreased plasma vitamin E levels.
Project Dates:
July 1972–July 1986.
Financial Support:
East Tennessee State University; KTHRI (KTRB-041).

1447. OAK RIDGE NATIONAL LABORATORY, Building 4500S, P.O. Box X, Oak Ridge, Tennessee 37831.

Project Title:
Collection, Separation, and Elucidation of the Components of Cigarette Smoke and Cigarette Smoke Condensate.

Principal Investigators:
Jenkins, R.A.; Guerin, M.R.
Objective:
To act as a resource for tobacco-related studies at the National Cancer Institute (NCI) and the National Institutes of Health through direct assistance to NCI-supported projects; conduct research for development of instrumentation and methods for chemical characterization of cigarette smoke.
Methods or Approach:
Cigarettes are smoked under standard and more humanly relevant smoking parameters to expand the informational data base and to address specific issues. New analytical methods are developed to more accurately and/or cost effectively determine levels of toxic or carcinogenic constituents in smoke. Dosimetry/monitoring instrumentation is developed to more accurately characterize human smoke exposure.
Results to Date:
Comparison of smoke deliveries from cigarettes manufactured in the mid-1970s with modern counterparts indicates that there have been few significant changes in nitric oxide:tar ratios. A very high nicotine/moderate tar delivery Turkish tobacco has been identified that may be of some use in developing a commercially viable low tar/medium nicotine cigarette. Methodology employing the adsorptive resin Tenax for multicomponent characterization of mainstream and sidestream tobacco smoke has been developed. It has been demonstrated that it is relatively easy for mainstream smoke from a low tar, highly ventilated cigarette to become contaminated with the sidestream vapor phase. Also, use of Tenax resin for collecting the vapor phase of ambient tobacco smoke (ATS) has suggested that compositional changes in smoke occur with aging. New, more rapid and accurate procedures for determination of phenol and the carcinogen benzo(*a*)pyrene (BaP) have been developed. For a small group of U.S. commercial cigarettes, phenol deliveries ranged from 6 to 75 μg/cigarette, while BaP deliveries varied from 2 to 20 ng/cigarette. A new variable-puff smoking machine has been used to generate smoke under a variety of puff shapes and volumes. Relative concentrations of bulk constituents in the smoke did not change, but relative levels of minor constituents appeared to have changed considerably. An advanced model of an instrumental smoke monitor for human studies has been constructed and is being evaluated. The device is designed to measure the amount of smoke an individual generates when puffing on a cigarette.
Future Plans:
Development of instrumentation for the quantitative characterization of human smoke exposure is expected to continue, as is characterization of the deliveries of commercial cigarettes under more humanly relevant smoking conditions. Some resources will be directed toward development of methods for a more definitive characterization of ambient tobacco smoke.
Project Dates:
September 1967–continuing.
Financial Support:
NCI (Y01CP30508).

1448. STATE FARM INSURANCE CO., 760 Northwest Broad Street, Murfreesboro, Tennessee 37131.

Project Title:
Health Promotion With Spirometry Testing.

Principal Investigator:
Morris, J.
Objective:
To improve health of company employees by conducting periodic spirometric examinations; provide education for subjects with borderline or below normal results.

Methods or Approach:
Spirometry testing was begun about 2 years ago as part of physical examinations of insurance company employees to promote better health.
Results to Date:
Although data are not conclusive, spirometry of many smokers is borderline or in the questionable area of normal. Health education on a one-to-one basis is provided about quitting smoking and increasing or starting an exercise program.
Financial Support:
State Farm Insurance Companies.

1449. TENNESSEE STATE UNIVERSITY, Nashville, Tennessee 37203.

Project Title:
Binding of Benzo(*a*)pyrene Metabolites to DNA.

Principal Investigator:
Chen, F.-M.
Objective:
To provide detailed understanding on the mutagenic pathway of benzo(*a*)pyrene (BaP) by elucidating the basis for the stereoselectivity of trans-7,8-dihydroxy-anti-9,10-epoxy-7,8,9,10-tetrahydro-BaP (anti-BPDE), the possible ultimate carcinogenic metabolite, on DNA binding.
Methods or Approach:
Research will include (1) detailed spectroscopic studies (absorption, circular dichroism, linear dichroism, fluorescence) on (racemic) anti-BPDE modified natural and synthetic DNAs; (2) parallel studies on syn-BPDE to discover the basis for its lesser carcinogenic potency compared with its anti counterpart; and (3) studies using the (+)- and (-)-enantiomers from these studies for comparison with racemic results and published works on natural DNA to reveal the extent of stereoselectivity of each polynucleotide and sequence specificity of the enantiomers.
Results to Date:
Absorption spectral results indicate that the extent of covalent modification with this metabolite is roughly poly(dG):poly(dC) approximately equals poly(dG-dC):poly(dG-dC) > poly(dA):-poly(dT) approximately equals poly(dA-dC):poly(dG-dT) > poly(dA-dT):poly(dA-dT). Distinct stereoselectivities are exhibited by poly(dG-dC):poly(dG-dC) vs. poly(dG):-poly(dC) as revealed by the oppositely signed CD in the pyrene spectral region. Significant anti-BPDE modification occurs with the hexaminecobalt-induced Z-form poly(dG-dC):-poly(dG-dC), although not as extensively as in the corresponding B-form. The spectral characteristics of anti-BPDE bonded to these two forms are distinctly different, with the Z-form more closely resembling those of poly(dA):poly(dT).
Future Plans:
Research will quantitatively characterize the covalent adducts formed by reacting (+)- and (-)-anti-BPDE with various polynucleotides through enzymatic degradation, high performance liquid chromatography separation, and spectral identification of hydrolysis products so that the bases for sequence-dependent stereoselectivity can be rationalized.
Project Dates:
August 1981–July 1984.
Financial Support:
NCI (CA 29817).

1450. UNIVERSITY OF TENNESSEE, COLLEGE OF MEDICINE, 956 Court Avenue, Memphis, Tennessee 38163.

Project Title:
Lung Macrophages in Centrilobular Emphysema (Rats).

Principal Investigator:
Hoidal, J.R.
Objective:
To determine the roles of alveolar macrophages (AM) and polymorphonuclear leukocytes (PMN) in the development of emphysema.
Methods or Approach:
Cigarette smoking appears to alter the numbers and activities of AM and PMN in such a way that potential toxicity for lung tissue is increased. A model of emphysema has been developed that involves intratracheal administration of calcium chloride to hamsters fed the lathyrogen beta-aminoproprinitrile. Using this model, experiments have been designed that will determine the time course relationships between the number of AM and/or PMN in the lung, metabolic and enzymatic activities, and the development of emphysema. The effect of selective depletion of AM and/or PMN on the development of emphysema will also be determined. Findings will provide a better understanding of lung injury so that methods of interrupting the process can be designed and tested.
Results to Date:
Project is in a preliminary phase.
Financial Support:
NHLBI (HL 32329-02).

1451. USDA, ARS, UNIVERSITY OF TENNESSEE, Knoxville, Tennessee 37916.

Project Title:
Fertilization and Cultural Practices to Improve Tobacco Safety.

Principal Investigator:
Nichols, B.C.
Objective:
To reduce or eliminate pesticide residues on burley tobacco associated with controlling suckers by chemical means; produce tobacco with as low alkaloid content as possible consistent with profitable yield.
Methods or Approach:
Cooperate with the Regional Tobacco Growth Regulator Committee in the search for satisfactory compounds to control suckers. New chemicals and various combinations of chemicals with reduced rates of maleic hydrazide (MH) will be treated to determine if MH residues can be reduced while maintaining satisfactory sucker control. Combinations of MH and fatty alcohols will be tested along with combinations of any new chemicals discovered that are compatible with MH for sucker control. Analyses for MH residues will be made. Rates of fertilizer nitrogen will be used to determine if low alkaloid tobacco can be produced while maintaining acceptable yields. Two standard varieties, Virginia 509 and Kentucky 17, will be grown, with N rates varying from 75 to 300 lb/acre. Plant population studies will be made with the Virginia 509 variety. Four population variables will range from approximately 6,000 to 12,000 plants/acre. In addition to agronomic data, analyses for alkaloids content will be made.
Results to Date:
Several sucker control compounds were evaluated for degree of phytotoxicity and efficacy as part of the Regional Growth Regulator Evaluation Program. Studies demonstrated that

application of a fatty alcohol (FA) followed 10 days later by an application of maleic hydrazide gave excellent sucker control over a 4- to 5-week period. Such treatment would facilitate earlier topping and later harvesting to produce higher yields of better quality tobacco with lower MH residues. Granular MH formulations gave good control of sucker growth and may provide a more efficient, less expensive means of sucker control for farmers. Studies with local systemic types of compounds indicate that, with proper application, excellent sucker control is maintained throughout the harvesting period. Potential problems exist in establishing small grain cover crops following use of local systemic sucker control agents. Herbicide residue studies have demonstrated that establishment of small grain cover crops is retarded in dry seasons following use of Prowl or Prowl plus Devrinol. Preliminary experiments on banding of fertilizer showed that the amount of fertilizer necessary and the time and labor involved could be reduced over that required for conventional broadcasting of fertilizer. Buildup of salt residues is a potential problem with banding of fertilizers.

Project Dates:

October 1979–September 1984.

Financial Support:

USDA (TEN00583).

1452. VANDERBILT MEDICAL CENTER, Health Promotion Center, S-1219 Medical Center, Nashville, Tennessee 37232.

Project Title:

Smoking Cessation and Exercise.

Principal Investigator:

Heim, C.R.

Objective:

To determine if exercise leads to improved long-term cessation rates after a standard group smoking cessation program; determine the relationship between smoking cessation and level of exercise participation and change in fitness status with time.

Methods or Approach:

Graduating participants in an American Lung Association Freedom From Smoking clinic will be randomized into exercise and control groups. Each will have a baseline fitness assessment, 6-month assessment of smoking status, and 12-month assessment including fitness test. Subjects in the exercise group will be asked to participate in a Vanderbilt-sponsored exercise class three times/week (walking/jogging, bicycling, or aerobics).

Results to Date:

Project is in a preliminary phase.

Project Dates:

January 1985–January 1987.

Financial Support:

AHA; ALA.

1453. VANDERBILT UNIVERSITY, SCHOOL OF MEDICINE, Nashville, Tennessee 37232.

Project Title:

Purified Human Enzymes and Carcinogen Metabolism.

Principal Investigator:

Guengerich, F.P.

Objective:

To provide data on the enzymatic bioactivation and detoxification of potential toxic compounds in humans by using purified preparations of human cytochrome P-450, NADPH-cytochrome P-450 reductase, and epoxide hydrolase to answer questions about the reactions catalyzed by these enzymes and the incidence of various forms of these enzymes in human populations.

Methods or Approach:

Research will (1) obtain additional preparations of the enzymes from human liver; (2) compare some of the physical, chemical, and immunological properties to corresponding enzymes isolated from rats and rabbits; (3) examine abilities of individual human cytochrome P-450 to activate procarcinogens to metabolites irreversibly bound to DNA and protein; (4) examine activities in surgical biopsies; (5) examine metabolic profiles of benzo(*a*)pyrene and other carcinogens and substrates and elucidate the role of epoxide hydrolase in human systems; (6) compare the enzymes in different humans using sodium dodecyl sulfate polyacrylamide electrophoresis coupled with peroxidase-antiperoxidase visualization of antibody binding; (7) use the above technique in conjunction with peptide mapping to identify common antigenic sites of human enzymes; (8) develop monoclonal antibodies to individual forms of the human enzymes; (9) develop competitive radioimmune or enzyme-linked immune assays for individual forms of the human enzymes; and (10) localize the enzymes in human tissues using immunohistochemical techniques.

Results to Date:

Results are not yet available.

Project Dates:

July 1981–1984.

Financial Support:

NCI (CA30907-04).

1454. VANDERBILT UNIVERSITY, Department of Pharmacology, Nashville, Tennessee 37232.

Project Title:

Cholinergic System, Sperm Motility and Male Fertility.

Principal Investigator:

Rama Sastry, B.V.

Objective:

To delineate the role of acetylcholine (ACh), opioid peptides, and substance P (SP) in sperm motility and in three membrane systems.

Methods or Approach:

Nicotine may block cholinergic receptors on spermatozoa and thereby produce immotile sperm. The effects of nicotine and various pharmacological agents on sperm motility index of human ejaculated sperm were studied.

Results to Date:

Cholinergic agonists (pilocarpine), opiate receptor antagonists (naloxone), SP antagonists (D-pro^{2}, D-tyr^{7,8}-SP), and Ca^{+} channel blocking agents (verapamil) increased motility index (MI) of human spermatozoa at 4 hours, while selective choline acetyltransferase inhibitors, SP, and leucine encephalin decreased MI. Effects of nicotine on sperm motility are being studied. Findings will be useful in (1) evaluating the role of choline acetyltransferase-acetylcholine, carnitine acetyltransferase-acetylcarnitine, phosphatidylinositol-phosphatidic acid, and phospholipid N-methyltransferase systems in sperm motility; (2) understanding infertility in those who ejaculate immotile sperm; (3) explaining transient infertility in male smokers and men exposed to dibromochloropropane; and (4) developing antifertility agents.

Project Dates:

April 1984–March 1987.

Financial Support:

NICHD (HD10607-09).

1455. VANDERBILT UNIVERSITY, Department of Pharmacology, Nashville, Tennessee 37232.

Project Title:
Maternal Smoking and Blood Concentrations of Amino Acids in Umbilical Arteries and Veins.

Principal Investigator:
Rama Sastry, B.V.

Objective:
To (1) determine amino acid profiles in placenta, umbilical arterial blood, and umbilical venous blood from smoking and nonsmoking mothers; (2) develop methods for amino acid profiles by high performance liquid chromatography (HPLC); (3) determine role of endothelial cells in acetylcholine (ACh)-induced relaxation of placental vasculature and in decreased resistance to fetal blood flow; (4) determine levels of 5-hydroxytryptamine (5-HT) that causes vasoconstriction of placental vasculature and in umbilical blood; and (5) determine level of nicotine N-oxide, a metabolite of nicotine, that may accumulate in fetal blood.

Methods or Approach:
Blood samples from umbilical arteries and veins from smoking and nonsmoking mothers were collected after delivery of the placenta. Plasma was separated immediately from blood samples and a sample of placental villous tissue and plasma samples were extracted for amino acids by HPLC. Effects of nicotine and related compounds were also studied on strips of umbilical chorionic and villous arteries.

Results to Date:
Methods were developed to separate free amino acids from placenta, umbilical blood, and venous blood and to obtain complete amino acid profiles using a Water's 840-HPLC amino acid analysis system. Preliminary experiments indicated that ACh was capable of relaxing umbilical veins that were contracted by 5-HT. Intact endothelial cells were necessary for this effect. Results indicate a physiological role for release of ACh into placental circulation, and endothelial cells in placental vasculature of smoking and nonsmoking mothers are being evaluated. Development of HPLC methods for determination of 5-HT, nicotine, and nicotine N-oxide in umbilical blood of smoking mothers is in progress.

Future Plans:
Several samples from placentas of smoking and nonsmoking mothers will be studied. Arterial and venous ratios for each amino acid will be compared.

Project Dates:
January 1984–January 1987.

Financial Support:
CTR (1628).

1456. VANDERBILT UNIVERSITY, Department of Pharmacology, Nashville, Tennessee 37232.

Project Title:
Influence of Nicotine on the Release of Acetylcholine (ACh) in Human Placenta and Its Implications on Fetal Growth.

Principal Investigator:
Rama Sastry, B.V.

Objective:
To determine how placental transport of amino acids contributes to intrauterine fetal growth retardation.

Methods or Approach:
Mothers who smoke are more likely than nonsmokers to deliver infants who are underweight for gestational age and are at higher risk for complications of pregnancy-related placental necrosis, effects that may be explained by (1) placental deficits induced by nicotine and tobacco smoke components for amino acid transport, and (2) bioactivation of tobacco-related N-nitrosamines and covalent binding to vital molecules in placenta. The uptake of several labeled amino acids by isolated placental villus was measured in the presence and absence of several tobacco smoke components.

Results to Date:
According to a working model, nicotine depresses amino acid transport across placenta by interfering with placental ACh system, thereby causing deficits in ACh stimulation-amino acid coupling on the surface of the trophoblast facing maternal blood, and decreasing fetal blood flow by vasoconstriction of placental vasculature directly or through release of vasoactive substances in fetal circulation. 2-Benzoylethyltrimethylammonium and related choline acetyltransferase inhibitors inhibit uptake of neutral (α-aminoisobutyric acid (AIB), isoleucine), basic (lysine) and acidic (aspartic acid) amino acids by isolated placental villus. Nicotine and cyanide inhibited uptake of AIB and several other amino acids by placenta. A major part of cyanide inhibition is irreversible (64 percent); inhibition by nicotine is only partially irreversible (14 percent). Nicotine and 5-hydroxytryptamine caused vasoconstriction of umbilical, chorionic, and villus stem arteries, which was enhanced by ethyl alcohol.

Future Plans:
Investigations are in progress to determine whether nitrosonornicotine binds covalently to amino acid transport systems and to determine effects of dimethylnitrosamine and N-nitrosopyrrolidine.

Project Dates:
April 1983–June 1986.

Financial Support:
CTR (949C).

1457. VANDERBILT UNIVERSITY, HEALTH CARE RESEARCH PROJECT, 512 Godchaux Hall, Nashville, Tennessee 37240.

Project Title:
Psychosocial Correlates of Success in Smoking Reduction.

Principal Investigators:
Wallston, K.A.; Talley, P., Smith, M.

Objective:
To explore whether health locus of control beliefs and self-efficacy beliefs are better predictors of success in quitting or reducing cigarette smoking than either construct alone.

Methods or Approach:
It is hypothesized that value of smoking cessation would help potentiate predictive power of the two expectancy constructs. The study group (smokers who expressed a desire to quit or cut down) consisted of 30 who participated in formal cessation programs and 50 who were trying to quit on their own. Questionnaires were completed at baseline. At 3 and 6 months, phone interviews and mailed questionnaires were used to ascertain changes in smoking behavior and self-efficacy beliefs and to gather descriptive information about what was and what was not helpful during the quitting process.

Results to Date:
Analysis of 3-month data shows that the more people believe their health status is dependent on others, the more difficulty they have in reduction/cessation of smoking. This was also true for persons who reported "social pressure" as the reason for quitting. However, persons who put a high value on health, who believed their own behavior determined health status, and who were confident that they would be able to quit, were more

successful than persons with other combinations of the three constructs.

Project Dates:

February 1984–March 1985.

Financial Support:

Vanderbilt University.

1458. VANDERBILT UNIVERSITY, SCHOOL OF MEDICINE, Division of Clinical Pharmacology, Nashville, Tennessee 37232.

Project Title:

Effect of Smoking on the Endogenous Production of Prostacyclin and Thromboxane and the In Vivo Platelet Function in Man.

Principal Investigators:

Fitzgerald, G.A.; Murray, J.; Nowak, J., et al.

Objective:

To assess effect of smoking on endogenous production of thromboxane A_2 and prostacyclin, the eicosanoids that control platelet aggregability; evaluate relationship of changes in production of both eicosanoids to platelet function in vivo.

Methods or Approach:

The experimental approach is based on measurement of the rate of biosynthesis of thromboxane A_2 (TxA_2) and prostacyclin (PGI_2) using a highly sensitive and specific, noninvasive method that allows assessment of minor alterations in the in vivo synthesis of the eicosanoids by quantifying the excretion rate of their major urinary metabolites (2,3-dinor-6-keto-$PGF_1\alpha$ and 2,3-dinor-TxB_2, respectively) using gas chromatography coupled to mass spectrometry operating in the negative ion chemical ionization mode. In vivo production of TxA_2 and PGI_2 is assessed in nonsmokers and in chronic smokers (20 cigarettes/day) during smoking and withdrawal. Platelet function in vivo and in vitro is evaluated by measurements of β-thromboglobulin, platelet factor 4, circulating platelet aggregates, and ADP and epinephrine-induced platelet aggregation. As a pharmacological tool in estimation of a possible contribution of platelets to overall thromboxane formation, aspirin is employed at doses able to selectively inhibit thromboxane synthesis in platelets but not in tissues.

Results to Date:

Results to date demonstrate increased excretion of 2,3-dinor-TxB_2 in smokers, implying increased biosynthesis of TxB_2 compared with nonsmokers. Platelet factor 4 and circulating platelet aggregates do not appear to be altered in smokers compared with nonsmokers, but β-thromboglobulin levels were higher in smokers. Despite evidence for platelet activation in vivo, the aggregation response to ADP and epinephrine was lower in smokers and increased significantly during withdrawal. Rate of 2,3-dinor-6-keto-$PGF_1\beta$ excretion was similar in both groups. Low-dose aspirin treatment suppressed excretion of 2,3-dinor-TxB_2 in smokers below even the predosing levels in nonsmokers, implicating platelets as a source of increased TxA_2 formation. Data indicate that in vivo platelet thromboxane formation is increased in chronic smokers, but that biosynthesis of PGI_2 appears to be unaltered. Despite evidence for in vivo platelet activation, platelets are less susceptible to in vitro aggregation in chronic smokers.

Future Plans:

Studies will evaluate acute effects of smoking to determine whether (1) acute smoking results in activation of platelets in vivo; (2) there is corresponding release of thromboxane in the circulation; (3) platelet activation is accompanied by alterations in endogenous prostacyclin generation; and (4) all these possible events correlate with the concentrations of nicotine in circulating blood.

Project Dates:

September 1984–May 1986.

Financial Support:

NHLBI (HL 30400); AHA.

1459. VETERANS ADMINISTRATION MEDICAL CENTER, 1030 Jefferson Avenue, Memphis, Tennessee 38104.

Project Title:

Development of an Oral Leukoplakia Proneness Profile.

Principal Investigators:

Koski, O.R.; Mincer, H.H.; Wyatt, J.R.

Objective:

To determine the feasibility of developing an oral leukoplakia risk profile; identify those factors associated with an increased risk of developing oral leukoplakia and subsequent squamous cell carcinoma.

Methods or Approach:

Twenty-three subjects with nondysplastic leukoplakia, five with significant epitheliel dysplasia, and nine with squamous cell carcinoma have been compared according to several parameters with a like number of control patients. Data were gathered by physical examination to include general nutritional appearance; height, weight, ponderal index, upper arm circumference, and triceps skin-fold thickness; oral examination; social and medical history; tobacco, alcohol, and drug experience; a dietary questionnaire; a Cornell Medical Health Index Questionnaire; biopsy and cytology specimens; routine automated fasting blood chemistries (SMC-20); nonautomated serum studies for carotene, ascorbic acid, folate, iron-binding capacity, vitamin A, Vitamin B-13, thiamine, riboflavin, niacin, pyridoxine, chromium, cobalt, copper, zinc, manganese, and selenium; routine hemoglobin studies (Coulter); routine urinalysis and urine quantitations for creatinine, N-methylnicotinamide, thiamine, and riboflavin; enumeration of circulating T-lymphocytes by the rosette method; and circulating lymphocyte stimulation testing with phytohemagglutinin, concanavalin A, LPs, herpesvirus 1 antigen, and *Candida albicans* antigen.

Results to Date:

Patients with lesions tended to show (1) higher incidence of tobacco and alcohol use; (2) underweight by the various body weight indexes; (3) "poorer" dietary patterns with respect to protein ratio and vitamin intake (particularly vitamin A); and (4) lower levels of serum albumin, folate, and hemoglobin. This study is completed.

Financial Support:

VA.

1460. BAYLOR COLLEGE OF MEDICINE, Department of Pharmacology, Houston, Texas 77030.

Project Title:
^{32}P-Labeling Test for DNA Damage

Principal Investigator:
Randerath, K

Objective:
To develop and apply methods for DNA and RNA adduct analysis which do not require radioactive carcinogens.

Methods or Approach:
Methods include (1) exposure of DNA and RNA in vivo and in vitro to carcinogens; (2) purification of nucleic acids; (3) digestion to mononucleotides; (4) in vivo incorporation of ^{32}P-label into digestion products; and (5) chromatographic separation and detection of adducts.

Results to Date:
Many carcinogen–DNA and carcinogen–RNA adducts could be detected and quantitated by this newly developed method with great sensitivity (detection of a single adduct in $10^{[illegible]}$ to $10^{[illegible]}$ total nucleotides). The results of applying the method to DNA in liver and skin have been published. Recently, DNA adducts were detected by ^{32}P-labeling in human and animal tissues exposed to cigarette smoke or cigarette smoke components.

Future Plans:
Plans include extending the study to other compounds and establishing the correlations between nucleic acid binding and the carcinogenicity of chemicals. Use of this method as a prescreen for chemical carcinogens is also planned.

Project Dates:
May 1982–1987.

Financial Support:
NCI (CA 32157).

1461. BAYLOR COLLEGE OF MEDICINE, Department of Pathology, Houston, Texas 77030.

Project Title:
A Search for Preneoplastic Cell Markers in Human Sputum.

Principal Investigator:
Greenberg, S.D.

Objective:
To identify premalignant changes in pulmonary epithelial cells in sputum; establish definitive objective morphometric criteria for the identification of atypical bronchial epithelial cells in sputum.

Methods or Approach:
It is proposed that the pathogenesis of lung cancer occurs as a progressive pattern of bronchial epithelial atypias extending over a period of 10 to 20 years, with the first step being squamous metaplasia, followed in turn by mild, moderate, and severe epithelial atypia and culminating in carcinoma. It is suggested that by periodic cytologic sputum examination, individuals who are at high risk for development of lung cancer can be identified and counseled regarding cessation of smoking, transferred to a less hazardous occupational environment, and possibly treated with retinoids to prevent further progression of bronchial atypias. In addition, computer-assisted morphometric analysis might assist in the tedious, labor-intensive searches.

Results to Date:
Results show that the degree of cell alterations in bronchial epithelial atypia can be accurately monitored by computerized cell image analysis.

Financial Support:
NCI (5R01CA27313-03).

1462. BAYLOR COLLEGE OF MEDICINE, INFLUENZA RESEARCH CENTER, Houston, Texas 77030.

Project Title:
Effects of Social and Family Factors on Viral Respiratory Infection and Illness in the First Year of Life.

Principal Investigators:
Gardner, G.C.; Frank, A.L.; Taber, L.H.

Objective:
To use data from the Influenza Research Center to determine whether or not certain select social factors such as sex, race, income/education, family size, smoking exposure, and day care attendance affect illness at the level of viral infection.

Methods or Approach:
Data from the Houston Family Study (families enrolled prior to the birth of a child and followed prospectively) were analyzed for 1975 through 1980. A total of 131 infants were monitored from birth through the first year of life for respiratory viral infection and illness.

Results to Date:
There were no general patterns of association between viral infection and study factors, but there were several significant individual associations: excess influenza virus infection was found for black infants and infants with at least one sibling (especially those with school-age siblings), and rhinovirus infection rates were highest among girls attending daycare. No convincing differences for viral infection or respiratory illness were seen with parental smoking as an isolated factor; however, the highest incidence of pneumonia occurred in infants of nonemployed mothers who smoked. From 1975 to 1980, there were 11 episodes of pneumonia and 9 (82 percent) occurred in black infants of mothers who smoked.

Reference:
Gardner, G.; Frank, A.L.; Taber, L.H. "Effects of Social and Family Factors on Viral Respiratory Infection and Illness in the First Year of Life." *Journal of Epidemiology and Community Health* 38(1):42-48, March 1984.

1463. BAYLOR COLLEGE OF MEDICINE, Department of Neurology, 6501 Fannin NB 302, Houston, Texas 77030.

Project Title:
Neuromuscular Disease Due to Tobacco Use.

Principal Investigator:
Patten, B.M.

Objective:
To call attention to the possible adverse effects of nicotine on neuromuscular function.

Methods or Approach:
Five patients (aged 11 to 55) with 2 to 35 years of experience with tobacco use were studied to determine the relationship between tobacco use and neuromuscular complications. All subjects were heavy users: an 11-year-old female had smoked two packs of cigarettes/day for 2 years, a 28-year-old male had smoked four to seven packs/day for at least 7 years, and the others had used snuff or chewing tobacco throughout waking hours for 6 months to 35 years.

Results to Date:
In each case, there was unexplained neuromuscular disease with weakness and easy fatigability sometimes associated with shortness of breath, palpitations, and muscle wasting. Patients who decreased or stopped tobacco use noted some improvement. A review of the literature shows abundant clinical and experimental evidence that exposure to nicotine causes major adverse effects on components of the motor unit, and absorption of nicotine by smokeless tobacco use can produce blood levels higher than are usually found in heavy smokers. Failure to improve after tobacco use is discontinued does not exclude the diagnosis because permanent damage to the nervous system may have already occurred.

Future Plans:
A more detailed study of weaknesses induced by snuff and chewing tobacco is planned.

Reference:
Patten, B.M. "Neuromuscular Disease Due to Tobacco Use." *Texas Medicine* 80:47-51, April 1984.

1464. CHILDREN'S HEART INSTITUTE OF SOUTH TEXAS, P.O. Box 3966, Corpus Christi, Texas 78404.

Project Title:
Brooks County Study.

Principal Investigator:
Phillips, G.T.

Objective:
To assess cardiovascular disease risk factors in children aged 0 to 18 years in a predominately Hispanic community.

Methods or Approach:
Research method is based on the Bogalusa Heart Study model. Data collected include cholesterol levels, triglycerides, lipoprotein levels, skinfold thickness, blood pressure, insulin levels, and lifestyle questions on alcohol use and smoking habits.

Results to Date:
Project is in a preliminary phase.

Future Plans:
A 5-year study of 2,500 children in Brock County, Texas, will be conducted.

Project Dates:
November 1984–October 1985.

Financial Support:
Texas Planning Council on Developmental Disabilities.

1465. DOD, DEPARTMENT OF THE AIR FORCE, SCHOOL OF AEROSPACE MEDICINE, Clinical Sciences and Biometrics Division, Brooks Air Force Base, San Antonio, Texas 78235.

Project Title:
Multivariate Approaches to the Detection of Asymptomatic Coronary Artery Disease.

Principal Investigators:
Tolan, G.D.; Honck, P.; Hickman, R., et al.

Objective:
To collect risk factor information on air crewmen in order to develop equations to predict which aviators in the apparently healthy flying population have significant coronary artery disease.

Methods or Approach:
Risk factor information is collected systematically on all air crewmen referred to the Aeromedical Consultation Service at the USAF School of Aerospace Medicine. The information collected includes family, social, and medical histories, blood lipids (including assessment of high density lipoproteins), glucose tolerance tests, serum enzymes, trace elements, serum cortisol levels, radioimmunoassay thyroid profile, body composition, pulmonary function screening, and ECG evaluations including treadmill exercise stress testing and Holter monitoring. When indicated, thallium-201 cardiac imaging and left heart catheterization including coronary arteriography are performed. These data are correlated with the results of coronary arteriography for the purpose of developing multivariate risk function formulas for immediate risk. Long-term followup studies of all patients including those not subjected to coronary arteriography are used to develop methods of predicting long-term risk for subsequent coronary events.

Results to Date:
In asymptomatic male aviators (aged 30 to 60 years), age and ratio of total cholesterol to high density lipoprotein cholesterol are most highly correlated with degree of coronary artery disease found on angiography. After removing the effect of age and this ratio, no statistically significant additional variance is explained by other risk factors. The ratio of total cholesterol to HDL cholesterol is itself strongly correlated with age, smoking, exercise, weight, and fasting blood glucose while weakly correlated to beer and wine consumption, but not spirits consumption. Preliminary findings suggest that cardiac fluoroscopy for calcium or abnormal wall motion is a very sensitive, if not specific, index for coronary artery disease even when ECG and thallium stress tests are normal.

Project Dates:
February 1971–continuing.

Financial Support:
USAF.

1466. HEALTH CARE STUDIES AND CLINICAL INVESTIGATION ACTIVITY, Fort Sam Houston, Texas 78234.

Project Title:
Evaluation of the Army Physical Training and Weight Control Programs.

Principal Investigators:
King, J.M.; O'Brien, D.E.; Mangelsdorff, A.D.

Objective:
To evaluate the effectiveness of physical training and weight control programs experienced by Army medical personnel, assess medical department impacts on these efforts.

Methods or Approach:
Data were collected on performance on the Army Physical Readiness Test, percent of body fat, and self-reported exercise history, demographics, lifestyle, attitudes, and perceptions.

Results to Date:
It was found that smokers were significantly less successful than nonsmokers on the Army Physical Readiness Test.

Project Dates:
September 1982–September 1983.

Financial Support:
USA.

1467. SOUTHWEST FOUNDATION FOR BIOMEDICAL RESEARCH, P.O. Box 28147, San Antonio, Texas 78284-9950.

Project Title:
Carcinogen Metabolism in the Cigarette Smoking Baboon.

Principal Investigators:
Marshall, M.V.; Rogers, W.R.; Carey, K.D., et al.

Objective:
To determine biochemical risk factors for development of lung cancer associated with cigarette smoking.
Methods or Approach:
Chronic cigarette-smoking baboons are compared with novice cigarette smokers to determine effects of acquisition of smoking on metabolism of benzo(*a*)pyrene (BaP) by pulmonary alveolar macrophages (PAMs) and bronchial epithelial cells (BECs). Cells are also utilized to activate carcinogens identified in tobacco smoke in a cell-mediated mutagenicity assay with V79 cells as target cells. Extent of smoking is documented by measuring blood carboxyhemoglobin levels and by monitoring levels of urinary mutagens.
Results to Date:
A positive correlation was observed between production of urinary mutagens and blood carboxyhemoglobin levels in baboons. No difference in basal mutagenic activity was observed with PAMs lavaged from sham-puffing or cigarette-smoking baboons. PAMs from cigarette-smoking baboons activated the proximate mutagenic metabolite of BaP (7,8-dihydrodiol) to a greater extent than PAMs from sham-smoking baboons. When sham-smoking baboons began smoking, this activity was elevated but to a lesser extent than that observed in chronic cigarette smokers.
Future Plans:
Both groups of animals will stop smoking, and pulmonary activation of carcinogens and urinary mutagens will be monitored. Both groups will resume smoking to compare effects of long-term and short-term cigarette smoking on pulmonary activation of carcinogens and urinary mutagens.
Project Dates:
August 1983–February 1986.
Financial Support:
NCI.

1468. TEXAS COLLEGE OF OSTEOPATHIC MEDICINE, Camp Bowie at Montgomery Street, Fort Worth, Texas 76107.

Project Title:
Use of Animal Model to Detect Subjective Symptoms of Withdrawal From Chronic Nicotine.

Principal Investigators:
Harris, C.M.; Emmett-Oglesby, M.W.; Lal, H.
Objective:
To (1) establish a pentylenetetrazol (PTZ) discrimination method for detecting withdrawal from nicotine (training rats to discriminate PTZ and testing whether withdrawal substitutes for PTZ-induced internal discriminable stimulus); (2) test whether drugs can block withdrawal-induced, PTZ-like, internal stimulus using nicotine, diazepam, clonidine, and mecamylamine (3) test whether drugs can elicit withdrawal-induced stimulus using mecamylamine (nicotinic receptor antagonist), R015-1788 (benzodiazepine receptor antagonist), and naloxone (opiate receptor antagonist); (4) determine effects of dose and duration of chronic nicotine treatment on magnitude of PTZ-like withdrawal stimulus; and (5) establish technique for maintaining rats in a chronic states of dependence, for use as a screening method for drug tests during withdrawal.
Methods or Approach:
Food-deprived male Long-Evans hooded rats are trained to press a lever for food reinforcement. Presses on one of two levers are reinforced after injection of PTZ; presses on the other lever are reinforced after saline injection. After rats are well trained, they are treated chronically with nicotine (injected s.c. at 8-hour intervals for >7 days) and then withdrawn. At various intervals after the last injection, rats are placed into the operant chambers and allowed to press either lever. Lever choice indicates whether the internal (subjective) state produced by withdrawal from nicotine is perceived as PTZ-like or not like PTZ.
Results to Date:
Withdrawal from nicotine (3.75 mg/kg/day for 15 to 21 days) produced an internal stimulus that partially substituted for the stimulus produced by PTZ (20 mg/kg). The withdrawal stimulus was blocked by diazepam and could not be elicited by mecamylamine (5 mg/kg) given immediately after last nicotine injection. Spontaneous withdrawal, measured at 8, 24, and 48 hours after last nicotine dose, had a stimulus intensity equivalent to a 10 mg/kg dose of PTZ. This withdrawal stimulus was additive with the stimulus produced by PTZ.
Future Plans:
Rats will be trained to discriminate 10 mg/kg PTZ, and tests will be conducted to determine whether the lower training dose increases sensitivity of the paradigm.
Project Dates:
January 1984–continuing.
Financial Support:
Texas College of Osteopathic Medicine.

1469. TEXAS TECH UNIVERSITY, HEALTH SCIENCES CENTER, Department of Physiology, Lubbock, Texas 79430.

Project Title:
Cardiovascular Effects of Chronic Carbon Monoxide-Altitude Exposure.

Principal Investigators:
McGrath, J.J.; Kopetzky, M.T.; McDonagh, P.F., et al.
Objective:
To determine effects of chronic exposure to carbon monoxide (CO) and to CO combined with altitude on the cardiovascular system of rats.
Methods or Approach:
Although it is known that chronic exposure to CO at high altitude produces pronounced physiological changes in humans and animals, there is little information available on the cardiovascular effects produced by these two stressors in combination. Laboratory rats are being exposed for 6 weeks to ambient atmospheric pressure (amb), CO at amb (amb + CO), altitude (alt), and CO at alt (alt + CO). The inhalation system consists of four steel barometric chambers, each sealed with a circular plexiglass door that permits viewing and servicing of animals. CO from commercial, high pressure cylinders is delivered into the chamber system via a mass flow controller. Chamber CO concentrations are continually monitored with a Beckman NDIR analyzer, and altitude is measured and controlled with an altitude system. Ranges being investigated are from 9 to 500 ppm CO and from 5,200 to 15,000 feet altitude. Changes in body weight, organ weights, and cardiovascular status are being evaluated.
Results to Date:
Effects of alt + CO on electrocardiogram (ECG) and heart weight (HW) were evaluated in rats exposed to amb, amb + 500 ppm CO, 15,000 feet alt, or 15,000 feet alt + 500 ppm CO. ECGs were taken under fluorothane anesthesia. Animals were killed and HW determined. Carboxyhemoglobin values were 36.2 percent ±3.5 and 34.1 percent ±3.9 in amb + CO and alt + CO, respectively. Hematocrits were 54±1, 77±[illegible], 68±1, and 82±1 percent, respectively, in amb, amb + CO, alt, and alt + CO groups. Mean electrical axes shifted 33.2° left in amb + CO, 30° right in alt, and 116.4 ° right in alt +

CO. Whereas CO increased left ventricular weight [illegible] increased right ventricular weight. alt + CO increased both. ECG changes were consistent with changes in HW. Results indicate that CO inhaled at ambient altitude causes a left electrical axis deviation, while CO inhaled at high altitude exacerbates the known phenomenon of right electrical axis deviation.

Future Plans:

The lowest altitude and lowest concentrations of CO at which significant effects can be detected will be determined, and the resistance to CO stresses in animal hearts will be assessed in vitro.

Project Dates:

March 1984–February 1987.

Financial Support:

Health Effects Institute.

1470. TRINITY UNIVERSITY, Department of Chemistry, 715 Stadium Drive, San Antonio, Texas 78284.

Project Title:

Biochemical Effects of Nitrogen Oxides and Nitrosyls.

Principal Investigator:

Doyle, M.P.

Objective:

To provide the chemical and biochemical basis for determination of the toxicity of nitrogen oxides, nitrosyls (including nitrites and nitrosamines), and dinitrogen compounds; develop a comprehensive mechanistic understanding of the diverse transformations of the substances in biochemical systems.

Methods or Approach:

Electron transfer processes with metalloproteins are recognized as primary effects resulting from animal and human exposure to the majority of these classes of compounds. The nature of electron transfer processes is revealed in kinetic investigations of hemoprotein oxidations by nitric oxide, the nitrite ion, alkyl nitrites, and N-nitrosyl derivatives. Both oxyhemoglobin and deoxyhemoglobin are employed, as are cytochrome c and hemerythrin. Kinetic rate constants and the specific events in the electron transfer step are determined from composite effects of dioxygen concentration, acidity, and substrate access to the metal center on reaction kinetics. Product analyses reveal reaction stoichiometry. Design and use of model systems is incorporated into the investigations.

Results to Date:

Decomposition of trioxodinitrate(II), formally the hydrate of the nitric oxide dimer, occurs by rate-limiting dissociation of the nitric oxide radical anion, and the chemistry proposed for this reactive species affords a rational explanation of the oxidative characteristics generally attributed to nitric oxide. Alkyl nitrite oxidation of ferrohemoproteins have been established as inner-sphere electron transfer processes. Nitrite ion oxidations of oxyhemoglobin are catalyzed by a peroxide–methemoglobin complex. The rate constant for the exceptionally rapid reaction between nitric oxide and oxymyoglobin has been confirmed by alternative methodologies. Investigations of the oxidative reactions of arenediazonium salts have revealed a novel process for electron transfer from hemoglobin through a channel to the heme pocket.

Future Plans:

Ongoing investigations are expected to reveal the link between the nitrous acid radical anion and the oxidative and reductive behavior of nitric oxide and the action of nitrite reductases. The relationship between the peroxidase activity of methemoglobin and autocatalytic oxidations of hemoproteins will be established.

Project Dates:

April 1982–continuing.

Financial Support:

NIEHS (ES01673; ES03609).

1471. UNITED STATES AIR FORCE MEDICAL CENTER, Department of Obstetrics and Gynecology, Wilford Hall, Lackland Air Force Base, San Antonio, Texas 78236.

Project Title:

Passive Smoking and Thiocyanate Concentrations in Pregnant Women and Newborns.

Principal Investigators:

Hauth, J.C.; Hauth, J.; Drawbaugh, R.B., et al.

Objective:

To estimate the degree of cigarette smoke exposure in pregnant women who smoke, those passively exposed to smoke, and those not exposed; determine effect of smoke exposure on umbilical cord thiocyanate concentrations in newborns of these mothers.

Methods or Approach:

All patients studied had a term pregnancy, no significant medical or obstetric complications, and uncomplicated vaginal delivery. Serum thiocyanate was used to estimate exposure in smokers, passive smokers, and nonsmokers.

Results to Date:

Mean thiocyanate concentration (95 μmol/L) was significantly higher ($p < 0.001$) in smokers than in passive smokers (35.9 μmol/L) or nonsmokers (32.3 μmol/L). Maternal and umbilical mean cord thiocyanate concentrations were similar among smokers (95 vs. 72 μmol/L). Although umbilical cord levels in infants of passive smokers and nonsmokers were similar (26 vs. 23 μmol/L), both levels were significantly lower than those of smokers. There was an inverse relationship between umbilical cord thiocyanate concentration and birth weight ($p < 0.001$). There was no evidence that passive cigarette smoke exposure resulted in higher maternal or umbilical cord thiocyanate concentrations than found in nonsmokers.

Financial Support:

USAF.

Reference:

Hauth, J.C.; Hauth, J.; Drawbaugh, R.B., et al. "Passive Smoking and Thiocyanate Concentrations in Pregnant Women and Newborns." *Obstetrics and Gynecology* 63(4):519-522. April 1984.

1472. UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER, SCHOOL OF PUBLIC HEALTH, P.O. Box 20186, Houston, Texas 77225.

Project Title:

Air Pollution and Lung Cancer in Harris County, Texas.

Principal Investigators:

Buffler, P.A.; Stallones, R.

Objective:

To investigate the contribution of air pollution to mortality from lung cancer in Harris County, Texas.

Methods or Approach:

A cross-geographical analysis of lung cancer mortality for white male residents of Harris County for 1979 to 1981 is being made to assess the contribution of air pollution. Units of analysis include Harris County census tracts. Air pollution estimates were based on total suspended particulate monitoring data (1969-1971). Regression techniques will be used to examine the relationship between mortality rates and measures of air pollution while statistically controlling for variables that are known to be linked with excess lung cancer mortality, including age, smoking, and socioeconomic status.

Results to Date:
Final analyses are being made, but results are not yet available.

Project Dates:
October 1979–April 1984.

Financial Support:
EPA (CR 807108-01).

1473. UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER, SCHOOL OF PUBLIC HEALTH, P.O. Box 20186, Houston, Texas 77225.

Project Title:
Etiologic Study of Respiratory Cancer in Coastal Texas.

Principal Investigator:
Buffler, P.A.

Objective:
To evaluate the relationship of environmental factors in the incidence of respiratory cancer in Caucasian residents of the Texas gulf coast.

Methods or Approach:
A case–comparison interview study was conducted of lung and laryngeal incident cancer cases diagnosed among residents of six counties during a 5-year period (1976-1980). Comparison subjects were selected from the general population. Interviews were conducted with next of kin when incident cases were deceased. Variables in the questionnaire included residential and occupational histories, smoking history, alcohol use, medical history, and nutritional information on vitamin A consumption.

Results to Date:
Data analysis using multiple logistic regression technique is continuing and several manuscripts are being prepared for publication.

Project Dates:
October 1979–October 1982.

Financial Support:
NCI (N01CP91025).

1474. UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER, SCHOOL OF PUBLIC HEALTH, P.O. Box 20186, Houston, Texas 77225.

Project Title:
Occupational and Environmental Exposures in the Etiology of Adult Leukemia.

Principal Investigator:
Buffler, P.A.

Objective:
To evaluate the joint etiologic importance of occupational exposures, environmental exposures, and cigarette smoking among newly diagnosed cases of adult male leukemia in six Texas gulf coast counties.

Methods or Approach:
All cases of leukemia among adult male residents diagnosed between January 1983 and December 1986 are being ascertained. A case–control interview study will be conducted using two control subjects for each case, selected from the general population and matched for age and race. All cases will be confirmed histologically and classified by cell type.

Results to Date:
Project is in a preliminary phase.

Future Plans:
Analysis of data will be by histologic type whenever numbers permit. Interactions among primary risk factors will be examined using the logistic model.

Project Dates:
March 1984–February 1987.

Financial Support:
NCI (CA 34448).

1475. UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER, SAN ANTONIO, VETERAN'S ADMINISTRATION MEDICAL CENTER, 7703 Floyd Curl Drive, San Antonio, Texas 78284.

Project Title:
Elastase Activity of Human Peripheral Blood Monocytes.

Principal Investigators:
Collins, J.F.; Fine, R.

Objective:
To demonstrate elastase activity in human peripheral blood monocytes (precursors of alveolar macrophages); determine variations in level of activity in normal people and in people with emphysema.

Methods or Approach:
Peripheral blood mononuclear cells are separated from erythrocytes and neutrophils on Ficoll-Hypaque gradients and monocytes are partially purified by adherence to plastic dishes. Adherent cells are collected and an extract made by homogenization. The extract is assayed for elastolytic activity by solubilization of an insoluble (^{3}H)elastin substrate. Activity is expressed as μg elastin degraded/hour/mg extract protein.

Results to Date:
Normal peripheral blood monocytes contain an elastase activity that can solubilize 5 to 10 μg insoluble elastin/hour/mg protein. The activity has characteristics of a serine protease and the level is 3 to 15 percent that of neutrophils from the same person (two subjects had activity at least twice that of other subjects).

Future Plans:
Monocytes from other normal individuals and persons with emphysema will be examined for levels of elastase activity to determine if high monocyte elastase levels predispose to emphysema.

Project Dates:
November 1979–June 1987.

Financial Support:
VA.

Reference:
Fine, R.; Campbell, M.E.; Collins, J.F. "Elastolytic Activity of Peripheral Blood Monocytes." *Connective Tissue Research* 13:27-35, 1984.

1476. UNIVERSITY OF TEXAS MEDICAL BRANCH, GALVESTON, CANCER CENTER, J-20, Galveston, Texas 77550.

Project Title:
Primary Smoking Prevention Among Pediatric Aged Outpatients.

Principal Investigators:
Philips, B.U.; Parcel, G.

Objective:
To develop a health education program aimed at outpatients aged 3 to 5 years, which could be used in a physician's office or in a clinic and incorporates health education to influence children not to smoke.

Methods or Approach:
The program is composed of five stories and reinforcement

activities for each. The main emphasis is that smoke is harmful to the body. The activities associated with the stories are intended to bring parents and children together in the learning experience. The program is distributed through the primary care physician to ensure reinforcement for participating parents and children and to provide an efficient means for following patients. The Solomon four-group design will be used in clinical evaluation of the program.

Results to Date:
The program of instruction is developed and pilot testing of the material is underway. Results of formative evaluation are expected in early 1985.

Future Plans:
A clinical trial and 15-year followup is planned.

Project Dates:
July 1984–June 1995.

Financial Support:
University of Texas, Cancer Center; NCI (20643-06).

1477. UNIVERSITY OF TEXAS, SCHOOL OF ALLIED HEALTH SCIENCES, Galveston, Texas 77550.

Project Title:
Smoking Habits and Reported Illness in Two Communities With Different Systems of Social Support.

Principal Investigators:
Philips, B.U., Jr.; Bruhn, J.G.

Objective:
To determine the role of different systems of social support in abating the consequences of risk behaviors such as smoking on chronic diseases.

Methods or Approach:
A retrospective comparison of smoking habits and reported illness in Roseto, Pennsylvania, and Tecumseh, Michigan, will be made. For purposes of analysis, the population of Tecumseh was used as the standard for adjusting Roseto data. Data were adjusted for age and sex.

Results to Date:
Smokers in both communities and of both sexes had less education than nonsmokers. Smoking habits of husbands and wives were similar. No statistically significant relationship was found in either community between smoking and coronary heart disease, hypertension, or somatic complaints; however, cigarette smoking was more common among respondents with a history of peptic ulcers. In Roseto, these persons tended to be the heaviest smokers. Results are interpreted in light of a cohort effect and differing systems of social support in the communities.

Future Plans:
The study will be expanded to focus on cancer prevalence.

Project Dates:
January 1981–1983.

Financial Support:
University of Texas; NIMH (MH 20400-01).

1478. UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER, SCHOOL OF PUBLIC HEALTH, P.O. Box 20186, Houston, Texas 77225.

Project Title:
CNS Tumors and Occupational Exposures.

Principal Investigators:
Buffler, P.A.; Frankowski, R.F.; Correa, P.

Objective:
To evaluate the importance of environmental and occupational exposures among incident cases of histologically confirmed primary neuroglial tumors of the central nervous system (CNS).

Methods or Approach:
All cases of CNS tumors among male residents (aged 20 to 79) of coastal Texas or Louisiana diagnosed between January 1980 and December 1984 are being ascertained. A case–control interview study is being conducted of CNS cases and control subjects, who are selected from the general population of the two study areas and matched for age, race, and geographic area. Approximately 1.3 controls are selected for each case. Suspected risk factors, including occupational exposure, environmental exposure, and radiation exposure will be investigated. Lifestyle factors, such as smoking patterns, alcohol use, and dietary habits are characterized for cases and controls. It is estimated that 375 cases will be identified in the six-county Texas area and 275 in the 26-parish Louisiana area.

Results to Date:
Confirmation of disease by review of histopathologic or radiologic materials is being provided by consultant pathologists and radiologists. Cases diagnosed through mid-1984 have been ascertained and interviews of cases and controls are proceeding. Data from the two areas will be analyzed separately and together.

Project Dates:
October 1982–September 1985.

Financial Support:
NCI (CA 32584-03).

1479. UNIVERSITY OF TEXAS, HEALTH SCIENCE CENTER, SAN ANTONIO, Department of Cellular and Structural Biology, 7703 Floyd Curl Drive, San Antonio, Texas 78284.

Project Title:
Nicotine Receptors of LHRH Axon Terminals in the Median Eminence.

Principal Investigator:
Hagino, N.

Objective:
To examine the presence of nicotine acetylcholine receptors in the axon terminals containing LHRH in the median eminence; analyze the function of nicotine acetylcholine receptors.

Methods or Approach:
Sprague-Dawley rats are used. The following methods are applied: (1) nicotine uptake; (2) localization of nicotine (autoradiograph and immunocytochemistry); (3) (^{3}H)nicotine binding sites; (4) denervation; (5) analysis of neurotransmitters; and (6) membrane potentials.

Results to Date:
Results show that (1) cholinergic neurons outside the basal medial hypothalamus provide axon terminals into the median eminence; (2) nicotine acetylcholine receptors are present in the median eminence; (3) nicotine reaches the cell by way of nicotine acetylcholine receptors and by cell membrane permeability; and (4) nicotine increases nicotine binding sites and subsequently stimulates synthesis and release of catecholamines.

Future Plans:
Research will include basic studies at the neuroendocrine and cellular level, focusing on questions concerning the effect of smoking (nicotine) during pregnancy and lactation on infant and child health, particularly development of neuroendocrine function.

Project Dates:
January 1982–June 1985.

Financial Support:
CTR (1371 M).

1480. UNIVERSITY OF TEXAS, HEALTH SCIENCE CENTER AT HOUSTON, P.O. Box 20186, Houston, Texas 77225.

Project Title:
Diet, Alcohol, Tobacco, and 25-Year Risk of Cancer in Men.

Principal Investigators:
Shekelle, R.B.; Butler, P.; Nichoman, M.Z.

Objective:
To investigate prospectively the association between dietary variables (e.g., vitamins A and C, animal fat, animal protein, dietary cholesterol), consumption of alcohol (primarily beer and liquor), use of tobacco, and risk of malignant neoplasms in 2,107 middle-aged men participating in the Western Electric Health Study.

Methods or Approach:
Information about diet and use of tobacco and alcohol was obtained, with other information, in 1957-1958 at baseline examination. Participants were reexamined annually through 1969. Interim data on alcohol and tobacco use were obtained at each examination, and interim information about diet was obtained in 1959 and 1960. Followup for vital status and morbidity from cancer was completed in 1978, with only three participants lost to followup. Followup is expected to continue through the 25th year. Data will help determine whether dietary habits during middle-age affect risk of commonly occurring cancers (e.g., lung, colon, rectum, bladder) 10 to 15 years later.

Results to Date:
Results indicate that intake of dietary provitamin A, but not preformed vitamin A, is associated inversely with 19-year risk of lung cancer, both in univariate analysis and after adjustment for age and cigarette smoking.

Project Dates:
1957–continuing.

Reference:
Shekelle, R.B.; Liu, S.; Raynor, W.J., Jr., et al. "Dietary Vitamin A and Risk of Cancer in the Western Electric Study." *Lancet* 2(8257):1185-1190, November 28, 1981.

1481. UNIVERSITY OF TEXAS, HEALTH SCIENCE CENTER AT HOUSTON, Center for Health Promotion and Development, P.O. Box 20036, Houston, Texas 77225. PAN AMERICAN HEALTH ORGANIZATION, UNITED STATES-MEXICO BORDER HEALTH ASSOCIATION, El Paso Field Office, 6006 North Mesa, Suite 700, El Paso, Texss 79912.

Project Title:
Buena Vida Sin Fumar - Media/Community Demonstration.

Principal Investigators:
McAlister, A.; Stern, M.; Ramirez, A.

Objective:
To (1) develop, pretest, and implement theory-based, replicable media interventions for a defined population with high rates of smoking; (2) produce and disseminate media communications designed to model skills related to smoking cessation/prevention; (3) demonstrate theory-based, replicable community organization methods for increasing long-term effects of mass media interventions by providing interpersonal reinforcement and support for responses that promote smoking cessation/prevention and maintenance of nonsmoking behavior; (4) demonstrate methods for identifying and supporting smokers at high risk for continuing or adopting heavy smoking owing to deficits in stress coping resources; and (5) assess effects of media and two levels of community intervention.

Methods or Approach:
Smoking rates are relatively high among men in specific low income populations near the Mexican border in southwest Texas, and if current trends continue, rates of smoking-related cancer may increase relative to populations in which smoking rates among men have decreased. A partially randomized, longitudinal, quasi-experimental design will be constructed involving residents of eight selected locations where adults in approximately 3,500 households and approximately 18,000 students in 10 senior high schools will be invited to participate. Cigarette smoking and variables related to smoking will be measured over a 5-year period in household interviews and classroom surveys. In subsamples, two or three biochemical tests will be employed to supplement self-reported smoking. Three locations will provide control or comparison for assessing program effects in four locations where different media/community activities will be conducted. One location will serve as a control for the first 2 years before experimental programs to reduce smoking are introduced. Three levels of experimental activity will be established: (1) mass media programs only; (2) media and direct community organization and training to increase encouragement and reinforcement for responses specifically related to smoking cessation/prevention; and (3) media and community organization as above, with establishment of additional systems for more general social support for coping with stress. Methods will be based on theoretical principles from the behavioral sciences and will also be designed to correspond to meaningful policy options for local and regional planners. All program activities will be integrated into existing public health service structures. Data will be analyzed to estimate cost effectiveness of different levels of intervention; test for different experimental effects of significant intervening variables; and test models of sociopsychological processes related to smoking cessation/prevention.

Results to Date:
Project is in a preliminary phase.

Project Dates:
January 1985–January 1990.

Financial Support:
NCI (1R01CA38347).

1482. UNIVERSITY OF TEXAS, GALVESTON, SCHOOL OF ALLIED HEALTH SCIENCES, Shearn Moody Plaza, Galveston, Texas 77550.

Project Title:
Development of Positive Health Behaviors in Preschoolers.

Principal Investigator:
Bruhn, J.G.

Objective:
To (1) design a comprehensive preschool health education curriculum (PHEP) and teach it to 4-year-old children; (2) determine the health behaviors, attitudes, beliefs, and values of the mothers of the preschool children (ages 2, 3, and 4); (3) follow, at yearly intervals, the 4-year-old children who were taught the PHEP curriculum, as well as a comparison group of 4-year-old children who were not taught the PHEP curriculum; and (4) identify possible changes in the health behavior, attitudes, beliefs, and values of mothers and children over time.

Methods or Approach:
Baseline information was obtained on the health habits of 2-, 3-, and 4-year-old children and their mothers during the first

project year, prior to any interventions. The children's mothers were interviewed in the home using a structured interview schedule. The Parent Questionnaire was administered during each successive year to include parents of children who received the PHEP curriculum. In addition, other forms of evaluation, such as a followup questionnaire for kindergarten teachers and assessments of children's preference for health and safety behaviors, were administered each year. Efforts were made to assess both the parents' effects on the children and the children's effects on their parents resulting from the teaching interventions.

Results to Date:

Project has been completed. The curriculum was field-tested in approximately 15 different preschool situations in Texas and California. Data indicate that (1) there is no significant relationship between mothers' modeling of positive health behaviors and children's initiation and practice of positive health behaviors; (2) preschool children can be taught and learn positive health behaviors when the material is age-relevant and fun, and when they can practice what they learn; (3) there are few significant changes from year to year in mothers' health behaviors, attitudes, beliefs, or values; and (4) mothers are more likely to use preventive health services for their children than for themselves.

Future Plans:

A continuation of this project, entitled Development of Health Behaviors in Middle Childhood, will study the preschool children in the current sample for 4 additional years. In addition, it will extend knowledge of the influence of the family and peers on the development of health behaviors to an additional sample (ages 5 to 12) and compare health behaviors, attitudes, and beliefs of healthy children with those of chronically ill children of the same age, sex, and ethnicity.

Project Dates:

July 1979–1983.

Financial Support:

NICHD (DHHS 5R01 HD13101); Moody Foundation.

1483. UNIVERSITY OF TEXAS, HOUSTON, HEALTH SCIENCE CENTER, Department of Pharmacology, P.O. Box 20708, Houston, Texas 77025.

Project Title:

Colloidal Metal Carcinogenic and Toxic Action.

Principal Investigator:

Costa, M.

Objective:

To study the mechanisms of particulate metal-induced carcinogenesis in various tissue culture systems.

Methods or Approach:

Selected metal compounds having different cancer-causing activities will be compared for their uptake, subcellular localization and site of cellular action during the early stages of neoplastic transformation. Phagocytosis and distribution of the particulate metals will be studied in intact cells by means of light microscopy, video intensification, light microscopy (video recordings of living cells), electron microscopy, and elemental mapping with energy dispersive x-ray analysis integrated with transmission electron microscopy. Parallel biochemical studies will focus upon isolating and purifying cellular components to determine molecular metal binding sites. Metal concentrations in isolated cell fractions will be measured by means of x-ray fluorescence while crystalline structure of metal compounds in these fractions will be determined by powder x-ray diffraction. The biochemical and intact cell approach will also be used to study the effect of inhibitors that disrupt metal-induced carcinogenesis or that disrupt specific cellular functions (i.e., colchicine, dansylcadaverine, etc.). Studies will also focus upon correlating whether carcinogenic metals cause DNA repair, or induce mutations in mammalian cells. These and other studies will help determine whether metals are initiators and/or promoters of carcinogenesis.

Results to Date:

Results are not yet available.

Project Dates:

October 1980–1983.

Financial Support:

EPA (R808048).

1484. VETERANS ADMINISTRATION MEDICAL CENTER, BAYLOR COLLEGE OF MEDICINE, 2002 Holcombe Boulevard, Houston, Texas 77030.

Project Title:

The Effects of Chronic Cigarette Smoking on Cerebrovascular Responsiveness to 5 Percent Carbon Dioxide and 100 Percent Oxygen Inhalation.

Principal Investigators:

Rogers, R.L.; Meyer, J.S.

Objective:

To determine if cerebral vasoconstrictor responses to inhalation of 100 percent oxygen and cerebral vasodilator responses to 5 percent carbon dioxide are affected by chronic cigarette smoking.

Methods or Approach:

If smoking promotes cerebral atherogenesis as anticipated, the cerebral vessels in smokers would become rigid and show decreased vasomotor responsiveness to both oxygen and carbon dioxide. Chronic smoking effects on cerebrovascular responsiveness of volunteers at risk or not at risk for stroke were evaluated by serial measurements of cerebral blood flow using the ^{133}Xenon inhalation method. Resting gray matter blood flow values measured while breathing room air were compared with values measured during inhalation of either 5 percent carbon dioxide or 100 percent oxygen. Changes in values during carbon dioxide inhalation were used to estimate cerebral vasodilator capacitance and those during 100 percent oxygen inhalation to estimate cerebral vasoconstrictor capacitance. Smokers were compared with nonsmokers, controlling for age, sex, and alcohol consumption.

Results to Date:

Results indicate that chronic smokers have both reduced vasodilator and vasoconstrictor responses when compared with nonsmokers of similar age and sex. Reductions occurred whether or not other risk factors for stroke were involved and appeared to be additive in subjects at risk. Vasodilator capacitance to carbon dioxide among smokers compared with nonsmokers was 48 percent in nonrisk subjects and 56 percent in subjects at risk; vasoconstrictor responses were reduced 24 percent in nonrisk smokers and 34 percent in smokers at risk. Subjects at risk were defined as having hypertension, hyperlipidemia, atherosclerotic heart disease, and/or diabetes mellitus.

Future Plans:

The effect of abstention from smoking on reducing rigidity of cerebral vessels and on the relationships between amounts and duration of smoking and reduced vasomotor reactivity will be investigated.

Project Dates:

January 1981–January 1991.

Financial Support:

VA; USPHS (NS09287).

1485. VETERANS ADMINISTRATION MEDICAL CENTER, BAYLOR COLLEGE OF MEDICINE, 2002 Holcombe Boulevard, Houston, Texas 77030.

Project Title:
Risk Factors for Cerebrovascular Disease Among Chronic Hypertensives.

Principal Investigators:
Rogers, R.L.; Meyer, J.S.

Objective:
To determine additional risk factors for cerebrovascular disease in a group of neurologically normal chronic hypertensive patients.

Methods or Approach:
A prospective analysis on the frequency of occurrence of possible risk factors (smoking, reduced cerebral perfusion levels, age, sex, duration of hypertension, and severity of hypertension) will compare smokers and nonsmokers to determine which factors increase the risk of cerebrovascular disease among hypertensive patients. Signs or symptoms of stroke, transient ischemic attacks, reversible ischemic neurological deficits, and/or multi-infarct dementia define the presence of cerebrovascular disease. Chi-square comparisons will be used to detect any differences in the distribution of possible risk factors between symptomatic and asymptomatic groups. To assess relative weighting factors of significant variables, a multivariate stepwise discriminant analysis will be utilized.

Results to Date:
Although final results are not yet available, preliminary data show that a number of the original volunteers have developed signs and symptoms of cerebrovascular disease including strokes, transient ischemic attacks, reversible ischemic neurological deficits, and/or multi-infarct dementia. Such data can offer insight into factors that predispose subjects at risk or compound the risk of stroke among hypertensive patients.

Future Plans:
The study will be continued over a 10-year period to accurately assess the important risk factors for stroke.

Project Dates:
January 1982–January 1992.

Financial Support:
VA; USPHS (NS09287).

1486. VETERANS ADMINISTRATION MEDICAL CENTER, 2002 Holcombe Boulevard, Houston, Texas 77030. BAYLOR COLLEGE OF MEDICINE, 1200 Moursund, Houston, Texas 77030.

Project Title:
Abstention From Cigarette Smoking Reverses Cerebral Hypoperfusion in Chronic Cigarette Smokers.

Principal Investigators:
Rogers, R.L.; Meyer, J.S.

Objective:
To determine whether cessation of smoking among long-term smokers reverses deleterious effects of smoking on cerebral arteries.

Methods or Approach:
Several designs and analyses are being utilized to investigate changes in cerebral blood flow following cessation of smoking. Cross-sectional analysis is used to compare cerebral blood flow levels among neurologically normal volunteers (nonsmokers, chronic smokers, and ex-smokers who had smoked for at least 10 years) to define any differences. A prospective study of long-term changes in cerebral gray matter blood flow among the three groups will be used to determine changes in cerebral perfusion and risk for cerebrovascular disease. Pre- and postcessation of smoking studies will be used to directly assess changes in cerebral perfusion following abstention from smoking.

Results to Date:
Preliminary results indicate that elderly volunteers who quit smoking have higher cerebral gray matter blood flow values than subjects who continue to smoke, but values remain slightly lower than for nonsmokers. Prospective analysis over a 4-year interval indicates that intermediate cerebral blood flow levels are maintained over extended periods of time. Abstention from smoking produces an increase in cerebral perfusion up to 2 years after quitting.

Future Plans:
Prospective studies will be continued to assess whether or not abstention from smoking will eventually cause cerebral perfusion levels to return to normal, and to determine what changes in risk for developing cerebrovascular disease occur in smokers who have quit compared with continuing smokers.

Project Dates:
July 1984–July 1994.

Financial Support:
Tenneco Inc.; J.S. Abercrombie Foundation.

1487. VETERANS ADMINISTRATION MEDICAL CENTER 2002 Holcombe Boulevard, Houston, Texas 77030.

Project Title:
Cigarette Smoking Decreases Cerebral Blood Flow Suggesting Increased Risk for Stroke.

Principal Investigators:
Rogers, R.L.; Meyer, J.S.

Objective:
To assess effects of chronic cigarette smoking on patency of cerebral vasculature.

Methods or Approach:
Effects on cerebral blood flow were investigated by measuring gray matter blood flow (133-xenon inhalation method) in 192 neurologically normal healthy volunteers. Of these, 108 were risk free, while 84 presented with risk factors for cerebrovascular disease (hypertension, atherosclerotic heart disease, hyperlipidemia, diabetes mellitus). Mean bihemispheric gray matter blood flow values were compared between the 117 nonsmokers, 14 moderate smokers (less than one pack/day), and 61 heavy smokers (more than one pack/day). All means were adjusted for age, sex, and level of alcohol consumption. Effects of cigarette smoking and other risk factors were assessed by analysis of covariance.

Results to Date:
There were significant reductions in blood flow values related to tobacco consumption and other risk factors for stroke, with a direct linear relationship between degree of reduced flow and number of cigarettes smoked/day. Chronic smoking in persons with other risk factors further reduced blood flow values in an additive manner compared with nonsmokers with the same risk factors. Smoking appears to be a potent risk factor that decreases cerebral blood flow, probably by enhancing cerebral arteriosclerosis.

Future Plans:
Future projects will determine (1) relationships between duration of smoking and reductions in cerebral blood flow; (2) effect of cessation on cerebral hypoperfusion; (3) long-term effects of tobacco consumption and interactions with normal aging processes; and (4) relationships between degree of

cerebral hypoperfusion secondary to smoking and risk for stroke.
Project Dates:
January 1981–January 1991.
Financial Support:
VA; NINCDS (NS09287).

1488. VETERANS ADMINISTRATION, 2002 Holcombe Boulevard, Houston, Texas 77211.

Project Title:
Clonidine in Tobacco Withdrawal: Two Phases, Open Pilot and Double Blind Controlled.

Principal Investigators:
Fann, W.E.; Pitts, W.M.
Objective:
To test the effectiveness of clonidine (CLN) in alleviating the symptoms of nicotine (tobacco) withdrawal.
Methods or Approach:
Clonidine was administered over a 10-day withdrawal period (0.1 mg p.o., three times/day for 7 days with tapering over 3 days) to 11 men who smoked at least a pack daily.
Results to Date:
Three men did not decrease cigarette use to 20 or less daily; two stopped smoking; the remaining 6 reduced consumption to 10 or less daily. Thus, 8 of the 11 subjects were partial abstainers. Comparison with smoking withdrawal results obtained by Shiffman-Jarvik (S-J) in their Smoking Withdrawal Symptom Questionnaire revealed a craving subscale curve approximating S-J total abstainers (return of craving subscore to baseline within 4-5 days) rather than the pattern that is characteristic of partial abstainers (elevation of craving subscores as long as partial abstinence is in progress). Anxiety and/or depression scores, determined by Zung and Hamilton ratings, did not significantly increase. Clonidine appeared to alleviate smoking withdrawal symptoms and permitted reduction or cessation of smoking in motivated subjects. The drug may relieve symptoms through action on CNS adrenergic mechanisms. Phase I, the open pilot study, was completed as summarized above. The double-blind, placebo-controlled phase will not be performed.
Financial Support:
VA.

Utah

1489. UNIVERSITY OF UTAH MEDICAL CENTER, RMCOEH, Building 512, Salt Lake City, Utah 84112.

Project Title:
Biological Effects of Smokeless Tobacco on Human Cells: An In Vivo Study.

Principal Investigators:
Livingston, G.K.; Reed, R.N.
Objective:
To test the hypothesis that exposure to smokeless oral tobacco does not cause detectable levels of genetic damage to somatic cells of the consumer.
Methods or Approach:
Cells tested include those most directly affected by oral tobacco (buccal mucosa cells and circulating blood cells) that may reflect possible systemic effects. The exposed group (n = 25) will be compared with a control group (n = 25) with respect to frequency of micronuclei in exfoliating buccal mucosa cells and in peripheral lymphocytes. The test is a rapid, sensitive, and quantitative indirect measure of chromosomal damage. Lymphocytes of both groups will also be cultured for analysis of sister chromatid exchange frequency, which has been found to be elevated in smokers. Positive results in either or both tests would indicate somatic cell genetic damage.
Results to Date:
Results are not yet available.
Future Plans:
Similar studies will be performed on smokers and nonsmokers and their offspring to test whether biological effects are found in children of smoking parents. In addition, effects in nonsmokers that may result from passive exposure to cigarette smoke will be investigated.
Project Dates:
July 1984–June 1985.
Financial Support:
STRC.

1490. UNIVERSITY OF UTAH, SCHOOL OF MEDICINE, Department of Family and Community Medicine, 50 North Medical Drive, Salt Lake City, Utah 84112.

Project Title:
Epidemiologic Investigation of Cancer in Utah.

Principal Investigators:
Lyon, J.L.; West, D.W.; Stanish, W., et al.
Objective:
To compare cancer incidence in Mormon versus non-Mormon residents of the State of Utah.
Methods or Approach:
A population-based cancer registry with data from 1966 onward provides cancer incidence information by site.
Results to Date:
Cancer incidence is estimated to be 20 percent less in Mormon vs. non-Mormon populations within the State. Major contributions to this decrease are made by cigarette-associated sites. However, unexplained differences exist in the incidence of uterine cervical cancer and stomach and colon cancer. Decreases in cancers unrelated to religion are also noted (e.g., pancreatic cancer).
Future Plans:
Registry records will be analyzed to better characterize differences by socioeconomic class and urban–rural residence. Case–control studies will help identify specific etiologic agents in ovarian cancer, cervical cancer, bladder cancer, colorectal cancer, and childhood cancers.
Project Dates:
Completed in 1982.
Financial Support:
NCI (NO1-CP 43382).
References:
(1) Lyon, J.L.; Gardner, J.W.; West, D.W. "Cancer in Utah: Risk by Religion and Place of Residence." *Journal of the National Cancer Institute* 65(5):1063-1071, 1980. (2) Lyon, J.L.; Gardner, J.W.; West, D.W. "Cancer Incidence in Mor-

mons and Non-Mormons in Utah During 1967-75." *Journal of the National Cancer Institute* 65(5):1055-1061, 1980. (3) West, D.W.; Lyon, J.L.; Gardner, J.W. "Cancer Risk Factors: An Analysis of Utah Mormons and Non-Mormons." *Journal of the National Cancer Institute* 65(5):1083-1095, 1980.

1491. UNIVERSITY OF UTAH, SCHOOL OF MEDICINE, Department of Family and Community Medicine, 50 North Medical Drive, Salt Lake City, Utah 84132.

Project Title:
Epidemiologic Investigation of Cervical Cancer in an Area of Low Incidence.

Principal Investigator:
Lyon, J.L.
Objective:
To determine factors relating to low incidence of cervical cancer in Utah, including sexual practice, religion, smoking, socioeconomic status, urban–rural residence, and medical care practices.
Methods or Approach:
A case–control study is conducted of cervical cancer patients identified through the Utah Cancer Registry and controls selected from the general population. An in-home interview is conducted with each subject regarding reproductive history and sexual practices, socioeconomic indicators, residential and medical history, religious affiliation, and smoking behavior.
Results to Date:
Cervical cancer incidence is very low in Utah Mormon women, and even lower in those who are regular participants in their church activities. Smoking is a strong risk factor for cervical carcinoma in situ, particularly in the younger age groups. Sexual behavior and socioeconomic indicators predict cervical cancer incidence, as has been demonstrated in numerous other studies.
Future Plans:
Proposals have been submitted for more detailed evaluation of smoking, douching, and herpes virus in cervical cancer.
Financial Support:
NCI (RO1-CA19871).

1492. UNIVERSITY OF UTAH, SCHOOL OF MEDICINE, Rocky Mountain Center for Occupational and Environmental Health, Building 512, Salt Lake City, Utah 84112.

Project Title:
Cigarette Smoke Interaction With Radon Daughters.

Principal Investigator:
Archer, V.E.
Objective:
To explore the interaction of cigarette smoking and radiation from radon daughters in the production of lung cancer among uranium miners.
Methods or Approach:
The age-related factors among smoking and nonsmoking uranium miners will be used in an attempt to assess the contribution of cigarette smoke. The interaction of cigarette smoke or smoke ingredients with alpha radiation in animals will be compared with epidemiological results in man. All human epidemiological studies relating to the interaction of cigarette smoke and radon daughters will be reviewed and compared with animal data. Since much of the data is conflicting, a theory will be developed that will attempt to explain all the animal and human data.
Results to Date:
Probably the most important finding to date is that the latent period for radon daughter-induced cancers is shorter among cigarette-smoking miners than among miners who do not smoke. This appears to result in a decreased incidence of lung cancer among older smokers, but a continued increase in incidence among nonsmoking uranium miners. It is suggested that the role played by cigarette smoking is mainly one of cancer promotion.
Project Dates:
February 1984–June 1985.
Financial Support:
University of Utah, School of Medicine.

1493. UNIVERSITY OF UTAH, GRADUATE SCHOOL OF SOCIAL WORK, Social Research Institute, Social Work Building, Salt Lake City, Utah 84112.

Project Title:
Prevention Services to Children of Substance-Abusing Parents.

Principal Investigator:
Kumpfer, K.
Objective:
To develop and test the relative effectiveness of three family-based prevention interventions in reducing substance abuse risk status of children (6 to 12 years of age) living with substance-abusing parents; identify and assess various etiological factors found in such families that contribute to generational transfer of substance abuse problems.
Methods or Approach:
The 2 x 4 factorial design method consists of four prevention/intervention groups: (1) parent training; (2) skills training for children; (3) family life skills training; and (4) no treatment controls. Groups are spread across two implementation sites (Salt Lake County Mental Health and Project Reality); curriculum and population differences and interaction of variables can thus be assessed. Covariate analyses will be completed for participant's sex, time of year program was run, number of parents participating from each family, number of sessions attended, and group facilitator. A needs assessment survey (between-group comparisons) should yield valuable etiological data on high-risk, drug-abusing, and normal families. Multiple measures are used to test effect of prevention interventions. Dependent variables are provided by standardized test batteries, Parent Knowledge of Child Discipline Principles questionnaire, parent and child interviews, demographic data questionnaire, and an alcohol and drug incidence and prevalence survey. The test battery is administered on a pre/post basis for experimental and no treatment control groups, and is employed as the dependent measure for the needs assessment part of the project. It is administered on a one-trial basis to clinic control, matched, and normal family groups.
Results to Date:
Final data are not yet available; however, preliminary analysis shows that when experimental families were compared with a group of non-substance-abusing families matched on age, education, and income, experimental families displayed (1) substantially higher levels of stress that are associated with mental health problems; (2) family profiles that closely approximate the "distressed" family; and (3) children who are more likely to be identified with behavioral problems, have restricted access to social resources, experience negative methods of child management, and hold higher expectations for performance on certain tasks than children of comparison families. Experimental families did show two areas of strength:

cohesion (negatively defined in clinical observations as leading to enmeshed and insular families) and expressiveness.

Future Plans:

It is anticipated that prevention services will be continued, utilizing the curriculum indicated by results to be most effective. Also, a design for a more complete needs assessment of substance-abusing families, including in vivo observations and video recordings of behavioral and interactional styles of families, will be submitted.

Project Dates:

September 1982–August 1985.

Financial Support:

NIDA (R18DA03888-03).

1494. USDA, Poisonous Plant Laboratory, 1150 East 14th North, Logan, Utah 84321.

Project Title:

Teratogenicity of *Nicotiana*.

Principal Investigator:

Keeler, R.F.

Objective:

To determine the teratogenicity of *Nicotiana* alkaloids and related compounds.

Methods or Approach:

Teratogenicity of *Nicotiana* alkaloids will be investigated in pigs.

Results to Date:

Nicotiana glauca, in which anabasine represents over 99 percent of the total alkaloid, is teratogenic in cattle and pigs. It produces terata in pigs identical to naturally occurring terata in pigs from maternal *Nicotiana tabacum* ingestion. The principal alkaloid of *N. tabacum*, nicotine, is inactive. Insult timing and terata morphology have been characterized. The principal alkaloid of *N. glauca*, anabasine, was found to be the teratogen of that plant.

Future Plans:

Other feeding trials in pigs of various analogs and of *N. tabacum* alkaloids will reveal the relative importance of anabasine and related compounds in the teratogenicity of *N. tabacum*.

Project Dates:

1974–1988.

Financial Support:

USDA.

1495. UTAH DEPARTMENT OF HEALTH, BUREAU OF HEALTH PROMOTION/RISK REDUCTION, P.O. Box 45500, Salt Lake City, Utah 84145.

Project Title:

Tobacco Use Among Selected Utah High School and Junior High School Students.

Principal Investigators:

Edwards, G.L.; Lindsay, G.B.; Lewis, L., et al.

Objective:

To determine tobacco (including smokeless tobacco) usage rates among selected Utah adolescents.

Methods or Approach:

Four school districts (three rural, one urban) were randomly chosen and one high school in each district was selected. One junior high school that feeds the selected high school was also selected. Students in the eight schools completed a one-page questionnaire.

Results to Date:

Survey data from 3,052 12- to 18-year-old students showed that 7.1 percent of both males and females reported having smoked in the last 24 hours; 38.2 reported having ever smoked (41.4 percent males, 34.6 percent females); 63.2 percent indicated having smoked for the first time prior to the age of 13. Smokeless tobacco use was primarily a male-dominated behavior; of the 3.6 percent who reported using smokeless tobacco in the last 24 hours, 92.5 percent were male. Ever use of smokeless tobacco was reported by 40.6 percent of males and 8.9 percent of females. Of those who had ever used smokeless tobacco, 68.5 percent reported doing so for the first time prior to the age of 14.

Future Plans:

Results will be analyzed for statistical significance, and educational efforts will be targeted accordingly. Annual followup surveys are anticipated.

Project Dates:

September 1984–continuing.

1496. VETERANS ADMINISTRATION MEDICAL CENTER, 500 Foothill Boulevard, Salt Lake City, Utah 84148.

Project Title:

The Health Decision Model in Coronary Artery Disease.

Principal Investigators:

Eraker, S.A.; Becker, M.H.; Kirscht, J.

Objective:

To evaluate the Health Decision Model (HDM), a third generation model of patient behavior that describes patient preferences and explains the determinants of decisionmaking.

Methods or Approach:

The HDM involves both social and psychological factors as well as decision analysis techniques involving tradeoffs between benefit/risk and quality/quantity of life. During the past year the evaluation of the HDM has involved two emphases: coronary artery disease and smoking cessation. Veterans with coronary artery disease scheduled for coronary angiography have been interviewed to determine the parameter estimates for a quality-adjusted life-year utility model along with other HDM variables. The assessments measure individual patient utilities for survival duration with and without angina. The HDM has also served as the basis for a minimum-contact smoking cessation program. Prior to a minimum-contact intervention, a questionnaire was administered that assessed current smoking practices of veterans. Smoking cessation rates were assessed 3 months following the intervention.

Results to Date:

Utility and HDM data have been collected on 25 of a projected sample of 80 patients undergoing angiography at the Ann Arbor VAMC. Most of the sample has been risk neutral and has been willing to trade off a substantial proportion of survival to be rid of their angina and related symptoms. Data analysis on 218 veterans enrolled in the prospective minimum-contact smoking cessation program support the HDM variables (such as psychosocial stress, health beliefs related to smoking, and desire to quit smoking) as being related to smoking cessation. The intervention group achieved significant smoking reduction, ranging from 15.9 percent for stopping to 52.4 percent for a reduction in smoking, as compared with the control group.

Financial Support:

VA.

1497. UNIVERSITY OF VERMONT, SCHOOL OF MEDICINE, Given Medical Building, Burlington, Vermont 05405.

Project Title:
Pathogenesis of Legionnaire's Disease.

Principal Investigators:
Beaty, H.N.; Davis, G.S.

Objective:
To define an animal model for the study of pulmonary infection with *Legionella pneumophila*; study the effect of factors such as smoking, corticosteroid therapy, and cytotoxic agents on the course of the disease.

Methods or Approach:
Bronchoalveolar lavage will be used to study the quantitative and qualitative aspects of cell recruitment in the course of the disease. Interactions between *L. pneumophila* and alveolar macrophages will be studied in vitro and in vivo. Changes in capillary permeability early in the development of inflammation will be studied using tracers such as horseradish peroxidase or ferritin. Animals that recover from infection will be rechallenged with the same or a different strain to assess the role of immunity in providing protection.

Results to Date:
The animal model studies are still in progress.

Project Dates:
August 1979–August 1985.

Financial Support:
NIAID (AI15903).

1498. UNIVERSITY OF VERMONT, Department of Physiology and Biophysics, Burlington, Vermont 05405.

Project Title:
Pulmonary Specialized Center of Research.

Principal Investigator:
Low, R.B.

Objective:
To define organ, tissue, and cell function as modified by specific etiologic agents of pulmonary fibrosis; provide the scientific basis for improving diagnosis and treatment.

Methods or Approach:
Analytical methods are used to describe pulmonary fibrosis in a carefully defined patient population and to determine effects of the disease process in lung physiology, morphology, and biochemistry. Analysis of cells and biochemical constituents of human bronchopulmonary lavage fluids is conducted. Animal models of fibrosis include bleomycin and aerosol inhalation of mineral particulates.

Results to Date:
The diagnostic and investigative usefulness of bronchoalveolar lavage fluid and cell analyses is demonstrated. Results also show the (1) contractile function of pulmonary interstitium and increased contractility in pulmonary fibrosis; (2) increased mineral content of lungs of human smokers, with suggestion of impaired clearance; (3) association of mineral deposits with pulmonary lesions; (4) interactions of lung macrophages and fibroblasts in culture, including altered fibroblast proliferation and collagen output; (5) endocytic pathways in lung macrophages; (6) molecular mechanism of action of cortisol on collagen production by lung cells; and (7) plasticity of collagen output by cultured lung fibroblasts.

Future Plans:
Studies will be continued in five program areas: (1) human studies, (2) pulmonary interstitial contractility, (3) mineral-induced lung injury, (4) lung cell interactions, and (5) collagen biochemistry.

Project Dates:
December 1981–1986.

Financial Support:
NHLBI (HL 14212).

1499. UNIVERSITY OF VERMONT, COLLEGE OF MEDICINE, Burlington, Vermont 05406.

Project Title:
Alveolar Macrophage Physiology in Interstitial Lung Disease.

Principal Investigator:
Davis, G.S.

Objective:
To characterize the clinical and pathophysiological expression of fibrotic lung disease in a carefully described patient population.

Methods or Approach:
The Specialized Center of Research (SCOR) has developed a comprehensive, organized, and systematic approach for the study of pathogenic mechanisms of human pulmonary fibrosis, involving nine different faculty and five different departments in the College of Medicine and one department in the College of Engineering, Mathematics and Business Administration. Of particular interest are fibrotic lung diseases associated with cigarette smoking and environmental exposure to inorganic particulates. Traditional approaches have been supplemented with novel approaches that may offer new opportunities for diagnosis and treatment and, by identifying causative agents, rational approaches to prevention. A second goal is to elucidate cellular pathogenic mechanisms of fibrosis through the study of lung cell interactions and with etiologic agents. Focus of SCOR is the fibrogenic process as it is expressed in different disease states, under the hypothesis that this process shares common pathogenic pathways in different diseases although caused by different etiologic agents.

Results to Date:
Results are not yet available.

Financial Support:
NHLBI (2P50HL14212-11).

1500. UNIVERSITY OF VERMONT, Given Building, Burlington, Vermont 05405.

Project Title:
The Effects of Nicotine and Other Constituents of Cigarette Smoke in Vertebral Blood Flow in Animal Models.

Principal Investigators:
Frymoyer, J.W.; Pope, M.H.

Objective:
To determine whether cigarette smoke or one of its constituents produces adverse effects on vertebral body blood flow, secondarily affecting nutrition of the disc, which is dependent upon diffusion.

Methods or Approach:
Epidemiologic studies have demonstrated an increased rate of low back pain and frank disc herniations in cigarette smokers. Experiments were conducted in physiologically stabilized dogs.

Vertebral blood flow was measured by a hydrogen washout technique from two adjacent vertebrae and diffusion of the ion through the disc by a probe placed within the intervertebral disc. Anesthesized dogs, monitored for physiologic parameters such as oxygenization, carbon dioxide content of blood, and stroke volume, have had vertebral body blood flow measured under resting conditions. Dogs were then challenged with varying doses of nicotine lactate and the same physiologic studies and hydrogen washout repeated. In a second experiment, rats were exposed to a smoke environment for a minimum of 2 to 4 weeks. Control (unexposed) and experimental animals were sacrificed at varying time intervals (up to 3 months) and intervertebral discs examined histologically for evidence of degeneration.

Results to Date:

A variable response to nicotine is found in experimental animals that is to some degree dependent on other physiologic parameters. In some animals, a significant diminution of vertebral blood flow accompanied by a diminution in diffusion of the hydrogen into the disc has been identified, while in other animals there has been no effect. Results are therefore inconclusive. In the short-term chronic experiments, some evidence of degenerative changes are identified in the intervertebral discs of animals exposed to smoking, but not in controls. Analysis is continuing.

Project Dates:

July 1982–October 1983.

Financial Support:

STRC.

1501. UNIVERSITY OF VERMONT, 235 Rowell, Burlington, Vermont 05405.

Project Title:

Organizing Social Influences to Prevent Smoking.

Principal Investigators:

Secker-Walker, R.H.; Flynn, B.S.; Worden, J.K.

Objective:

To reduce incidence of regular cigarette smoking among adolescents through a strategy based on education and communication principles, including (1) school programs for target group adolescents; (2) workshops in communication skills for parents, teachers, and other adults having contact with and influence upon adolescents; (3) coordinated mass media programs using local radio and newspapers; and (4) advice, initiative, and participation of local community advisory groups.

Methods or Approach:

Nine Vermont communities, with independent radio reception, have been divided into three groups, closely matched on the basis of demographics, size of fourth and fifth grade student bodies, and smoking behavior of the student cohort. Group 1 (three communities) was randomly assigned to receive the school program (usual treatment), communication skills workshops, mass media, and advisory group participation, with annual student surveys. Group 2 (three communities) was randomly assigned to receive the school program only, with annual student surveys. Group 3 was assigned to receive the school program only with student surveys in the first and fifth years. All data for individual students will be linked and can be compared with data obtained from the parent survey.

Results to Date:

Baseline survey data show that almost 30 percent of fourth and fifth grade students have been offered a cigarette; about 20 percent have smoked one or two; less than 2 percent smoke regularly. In general, attitudes of respondents toward smoking and perceived attitudes of friends are against smoking. Perceived parental smoking rates are comparable with smoking rates of men and women with blue-collar jobs in Vermont. Perceived attitudes of parents toward smoking are slightly more against smoking than attitudes of respondents and friends. Regarding communication patterns with parents, more mothers than fathers were perceived as talking to their fourth or fifth grader, listening carefully, helping with problems, and helping with making good decisions. Differences are most striking in helping with problems: mothers 57.3 percent, fathers 38.4 percent.

Project Dates:

September 1983–August 1988.

Financial Support:

NHLBI (5R01HL29643).

1502. UNIVERSITY OF VERMONT, 235 Rowell, Burlington, Vermont 05405.

Project Title:

Smoking Cessation During Comprehensive Health Care.

Principal Investigators:

Secker-Walker, R.; Bronson, D.L.; Flynn, B.

Objective:

To reduce prevalence of chronic lung disease through smoking cessation techniques introduced during comprehensive health care; reduce prevalence of cigarette smoking by 25 percent over the course of 1 year.

Methods or Approach:

Patients presenting for comprehensive health care examinations are counseled by a trained smoking cessation counselor at initial visit and again immediately before patients are seen by the physician (7 to 10 days later). Protocol for counseling includes (1) questionnaire about smoking behavior, motivation and intention to stop smoking, confidence in ability to remain abstinent; (2) health risk message personalized in relation to symptoms and pulmonary function test results; (3) exploration of balance of perceived benefits of smoking or not smoking and perceived barriers to quitting and remaining abstinent; and (4) development of a plan to quit smoking and rehearsal of skills for remaining abstinent. The plan for changing smoking behavior is reinforced by the physician, is entered on the patient's record, and is sent to them 2 weeks later with the rest of their record. At 3 months, continuing smokers are offered a variety of smoking cessation aids. Followup will be at 6 months and 1 year. Those who claim to have stopped smoking will have a sample of saliva tested for cotinine concentration. A total of 100 patients will be enrolled in experimental counseling and 100 in usual care.

Results to Date:

Preliminary data, based on 6-month followup of patients, suggest that individualized counseling is more effective in promoting cessation than usual practices in this comprehensive health care setting.

Project Dates:

July 1983–June 1985.

Financial Support:

NHLBI (PHS R18-31032).

1503. UNIVERSITY OF VERMONT, 235 Rowell, Burlington, Vermont 05405.

Project Title:

Smoking Prevention Through Mass Media and School Programs.

Principal Investigators:
Secker-Walker, R.H.; Worden, J.K.; Flynn, B.S.
Objective:
To design a set of three distinctly different antismoking media campaigns, aimed at young people in one of three developmental levels: before, during, and after puberty.
Methods or Approach:
Developmental levels correspond roughly to grades 5 and 6, 7 and 8, and 9 and 10. Message designs for each campaign will be developed independently by media consultants on the basis of diagnostic and formative research. With guaranteed exposure through paid advertising, each campaign will be scheduled to reach youth at proper developmental level at times when target groups are using the media. Four matching Standard Metropolitan Statistical Areas have been identified as study communities: Binghamton, New York; Burlington, Vermont; and Great Falls and Billings Montana. School systems matched between communities will participate in a school program currently being tested in Vermont, while also providing survey data. In all communities, a cohort of 5,000 students in grades five to seven will be provided with the smoking prevention program each year through grades 8 to 10. Great Falls and Binghamton will also receive mass media intervention. Annual formative and summative surveys will be conducted. Data collection techniques will allow description of individual patterns in changes in behavior, perception, and attitudes. In addition to self-report questionnaires, students will provide saliva samples, a subset of which will be analyzed for thiocyanate content.
Results to Date:
Project is in a preliminary phase; no results or findings are available at this time.
Project Dates:
September 1984–August 1989.
Financial Support:
NCI (R01CA38395).

1504. UNIVERSITY OF VERMONT, 235 Rowell, Burlington, Vermont 05405.

Project Title:
Smoking Cessation During Obstetric Care.

Principal Investigators:
Secker-Walker, R.H.; Mead, P.B.; Flynn, B.S.
Objective:
To reduce prevalence of chronic lung disease through smoking cessation techniques introduced in an obstetric care setting; reduce prevalence of cigarette smoking by 30 percent during the course of pregnancy.
Methods or Approach:
Women are counseled by trained smoking cessation counselors at the first three prenatal visits and followed throughout pregnancy with further contact by phone. Additional counseling is given at the 36th week and at a 6-week postpartum visit. Protocol for counseling includes (1) questionnaire about smoking behavior, attitudes toward smoking, motivation and intention of stopping, and confidence in ability to remain abstinent; (2) health risk message; (3) exploration of perceived benefits of smoking and not smoking and perceived barriers to stopping and remaining abstinent; (4) development of plan to change smoking behavior; (5) rehearsal of skills to remain abstinent; and (6) referral to self-help, group smoking cessation techniques, or home counseling. Smoking behavior is measured by self-report and by urinary cotinine in a random sample of study participants. Outcomes will be measured at 36th week of pregnancy and 1 year after delivery.
Results to Date:
Preliminary observations, based on first year data, indicate a significant change in smoking behavior among women being counseled compared with those not counseled, with cigarette consumption lower in counseled women.
Project Dates:
July 1983–June 1987.
Financial Support:
NHLBI (PHS R18-29957).

1505. VETERANS ADMINISTRATION MEDICAL AND REGIONAL OFFICE CENTER, 405/111, White River Junction, Vermont 05001.

Project Title:
Success Rate of Smoking Cessation Clinic Improved by Tailored Public Media Campaign.

Principal Investigator:
Mogielnicki, R.P.
Objective:
To determine whether the long-term smoking cessation rate of clinic-based behavior modification therapy can be increased by means of a mass media campaign directed at clinic participants.
Methods or Approach:
Smokers recruited through medical outpatient clinics of two similar Veterans Administration hospitals to participate in a smoking cessation study were randomly assigned to either a behavior modification clinic or a group that received a packet of smoking cessation material in the mail. After 2 years, an intensive media campaign on commercial television and radio, based on the behavior modification program, was targeted at the study population of one of the hospitals. Data were collected at enrollment and at 6 and 18 months after completion of clinic treatment or receipt of mailed kits, and included exhaled air sample for carbon monoxide content, venous blood specimen for thiocyanate level, and an extensive investigator-administered questionnaire.
Results to Date:
The 6-month abstinence rate for clinic participants measured by self-report, serum thiocyanate, and exhaled carbon monoxide was 36.8 percent in clinic participants exposed to media campaign, 20.2 percent in those participating in the clinic program only, and 10.6 percent in subjects who received mailed materials. The difference in cessation rates between clinic participants who were exposed and those who were not exposed to the media campaign was significant at the 0.05 level. Logistic analysis confirmed the benefit of the media campaign.
Future Plans:
Abstinence rates at 18 months will be analyzed and results published.
Project Dates:
July 1980–July 1984.
Financial Support:
VA (370).

1506. VETERANS ADMINISTRATION, N. Hartland Road, White River Junction, Vermont 05001.

Project Title:
Pharmacologic Approach to Cigarette Consumption Rates: Neuro Blockade.

Principal Investigators:
Balestra, D.J.; Dulac, J.; Mogielnicki, P.P.

Objective:
To assess whether commonly used drugs (clonidine, aminophylline, and propranolol) may alter cigarette craving and, therefore, cigarette consumption rates.

Methods or Approach:
Each subject is provided with his chosen brand of cigarette daily, and consumption is monitored by direct count the following morning. Cigarette consumption is monitored for 16 days: (1) 4 days of baseline; (2) 4 days receiving active drug or placebo (blinded); (3) a 4-day "washout" period; and (4) a final 4-day period of active drug or placebo (blinded).

Results to Date:
Fifteen subjects have been enrolled to date, of whom 11 completed the full 16-day study period; five have received aminophylline and placebo, four, propranolol and placebo, and two, clonidine and placebo. Each of the five subjects receiving aminophylline exhibited reduced cigarette consumption (mean 19 percent) while receiving active drug compared with placebo. Using the matched-pairs t test, reduction in cigarette consumption is significant at the 0.05 level.

Financial Support:
VA.

Virginia

1507. EASTERN VIRGINIA MEDICAL SCHOOL, P.O. Box 1980, Norfolk, Virginia 23501.

Project Title:
Phenotypic Analysis of Epithelial Cell Neoplastic Progression.

Principal Investigator:
Somers, K.D.

Objective:
To (1) study the multistage theory of carcinogenesis in epithelial cells; (2) identify chromosome changes with use of Giemsa banding techniques that are associated with transition from benign to malignant cell phenotype; (3) identify activated cellular oncogenes by DNA transfection; (4) identify membrane polypeptides acquired or lost as cells progress; and (5) determine ability of retinoids (natural and synthetic analogs of vitamin A) to arrest or reverse the process of epithelial cell neoplastic progression.

Methods or Approach:
The complete spectrum of neoplastic progression is exhibited by an epithelial cell line (NMuLi) derived from normal mouse liver. Cells at low passage (LP) in culture induce benign tumors (cystadenomas) when injected into mice; those at high passage (HP) induce adenocarcinomas. A variant (C1-A) derived from HP induces metastatic tumors. This cell culture system is being used as a model for studies on the nature of tumor cell progression.

Results to Date:
C1-A cells, which induce rapidly growing tumors, exhibit the completely transformed phenotype evidenced by a disordered growth pattern in vitro, and capacity to form colonies rapidly and efficiently in soft agar. HP and LP cells demonstrate a more ordered growth pattern and epithelial cell morphology in vitro, and either a reduced capacity or inability to grow in soft agar, respectively. Treatment of NMuLi cells with retinoic acid (RA) results in rapid cessation in rate and extent of growth and inhibits anchorage-independent growth of C1-A and HP cells. Cytogenetic analysis of NMuLi cell lines revealed increased heteroploidy and karyotypic instability associated with neoplastic progression. Examination of cytoskeletal elements by immunofluorescence microscopy demonstrated loss of actin cable and keratin intermediate filament organization with tumor cell progression. Using NIH/3T3 mouse cells as recipients in DNA transfection assays, it was shown that DNA extracted from NMuLi cells at LP, HP, and C1-A induce foci of morphologically transformed cells that seed rapidly growing tumors in nude mice. Analysis of metabolically labeled whole cell or membrane proteins by SDS gel electrophoresis demonstrated that LP and HP cells were indistinguishable with respect to ^{35}S-methionine polypeptide or ^{32}P-phosphoprotein content. In contrast, C1-A cells contain whole cell and membrane proteins and phosphoproteins not detected in LP and HP cells and lack additional polypeptides. RA treatment had no effect on biosynthesis of the proteins.

Future Plans:
Studies in progress include (1) analysis of keratin subunits in NMuLi cells by gel electrophoresis and immunoblotting and effect of RA treatment on cytokeratin filament expression; (2) relationship of transforming genes detected in NMuLi cells to known retroviral oncogenes; and (3) examination of glycoprotein synthesis and composition of NMuLi cells and effect of RA on expression of cell glycoproteins.

Project Dates:
July 1983–June 1986.

Financial Support:
STRC.

1508. NAVAL ENVIRONMENTAL PREVENTIVE MEDICINE UNIT-TWO, Naval Base, Norfolk, Virginia 23511.

Project Title:
Effectiveness of Isolation in the Reduction of Cigarette Smoking.

Principal Investigator:
Deaton, J.E.

Objective:
To determine the efficacy of a multimodal approach to smoking cessation that includes Restricted Environmental Stimulation Technique (REST), a technique in which external stimulation is reduced to a minimum.

Methods or Approach:
Using REST, patients were exposed to a series of taped messages dealing with various techniques designed to reduce smoking. Subjects spent 24 hours in a dark, sound-reducing chamber.

Results to Date:
Data for the four participants revealed a 68 percent reduction in smoking, and patients did not appear to experience any undue stress effects. Results obtained from the health scale 6 months after treatment indicated that patients experienced less tension, anxiety, and headaches over time, and had an increased ability to fall asleep. In terms of expressed attitudinal changes associated with smoking behavior, results indicated a significant change in orientation toward smoking: patients stated that they were more likely to maintain greater control over cigarette use. There was also significant change in that they were not as likely to feel that smoking is the result of an attempt to cope with negative emotions. Findings suggest that

the technique is effective in decreasing previous smoking patterns.

Reference:

Deaton, J.E. "Effectiveness of Isolation in the Reduction of Cigarette Smoking." *Military Medicine* 148:750-753, September 1983.

1509. RESEARCH DIMENSIONS, INC., 427 North Lee Street, Alexandria, Virginia 22314.

Project Title:

Adolescent Prevention Technology–Phase I.

Principal Investigator:

Hurley, J.

Objective:

To assess feasibility of developing new educational technology to teach adolescents how to avoid use of cigarettes, alcohol, marijuana, and pills.

Methods or Approach:

The new adolescent prevention technology will be based on successfully tested, research-based smoking prevention programs. The product resulting from successful activities in Phase I would be an approved curriculum model that would provide the conceptual framework for organization and future development of teaching units that could be incorporated in existing curricula at the elementary, junior high, and/or high school level by local classroom teachers. A report on feasibility of commercially marketing the curriculum will also be provided. The project will also attempt to provide a state-of-the-art drug use prevention curriculum based on existing successful smoking prevention techniques. Recognized experts in smoking prevention will be convened as an advisory panel to provide guidance in development of the new technology and to evaluate the resulting curriculum model.

Results to Date:

Project is in a preliminary phase.

Future Plans:

Phase II of the project would focus on development of instructional materials and evaluation instruments; pretest, revision, and final field test of materials; and production of materials for commercial test marketing.

Financial Support:

NIAAA (1R43AA06405-01).

1510. USDA, ARS, VIRGINIA POLYTECHNIC INSTITUTE, Blacksburg, Virginia 24061.

Project Title:

Assessment of Detoxification in Humans by Establishing Patterns of Excretory Urinary Conjugates.

Principal Investigator:

Webb, R.E.

Objective:

To (1) develop and refine methodology for urinary conjugates; (2) relate urinary conjugate levels (glucuronides, sulfate conjugates, glycine and glutamine conjugates, and mercapturic acids) in a population of healthy males to behavioral patterns (vegetarianism, use of drugs, smoking, caffeine and alcohol intake); and (3) determine range and variability of excretion levels of conjugates and index individuals into high and low profiles.

Methods or Approach:

A minimum of 200 adult male volunteers will provide 5-day food records and 3-day urine collections. Creatinine, free glucuronic acid, total glucuronides, free sulfate, sulfate conjugates, free glycine and glutamine, amino acid conjugates, and mercapturic acids will be determined in urine. Profiles of excretion patterns will be determined and related to food records and use of foreign compounds.

Results to Date:

Project is in a preliminary phase.

Project Dates:

January 1984–December 1986.

Financial Support:

USDA (VA-61455).

1511. VIRGINIA COMMONWEALTH UNIVERSITY, MEDICAL COLLEGE OF VIRGINIA, Department of Pharmacology and Toxicology, MCV Station Box 613, Richmond, Virginia 23298-0001.

Project Title:

Stereoselective Studies with (+)- and (-)-Nicotine.

Principal Investigator:

Aceto, M.D.

Objective:

To (1) study degree of tolerance to (+)- and (-)-nicotine that develops in the rat, emphasizing dose regimens that parallel nicotine intake of cigarette smokers; (2) determine degree of stereoselectivity with the isomers; (3) study development of physical dependence in the rat after chronic administration of (+)- and (-)-nicotine and, should it occur, characterize the abrupt withdrawal syndrome; (4) precipitate abstinence with antagonists if applicable; (5) measure in vivo cortical release of ^{3}H-noradrenaline after systemic administration of nicotine in doses equal to that of smokers; and (6) attempt to correlate blood and brain levels of nicotine with noradrenaline release.

Methods or Approach:

Effects on autonomic nervous system function (blood pressure, pulse rate, EKG, body temperature) and general functional status (motor activity, rotarod, coordinations) will be measured and effects on anxiety will be determined. Body weight and fluid intake will be monitored for each physiological or pharmacological response observed. Time course will be correlated with time courses of blood and brain nicotine levels. Noradrenaline and other brain amine release will also be determined.

Results to Date:

Project is in a preliminary phase.

Future Plans:

The interaction of nicotine with natural opiates will be studied.

Project Dates:

December 1984–November 1987.

Financial Support:

NIDA (DA 02384 04A2).

1512. VIRGINIA COMMONWEALTH UNIVERSITY, Richmond, Virginia 23220.

Project Title:

American Heart Association's Task Force For Cardiovascular Assessment in Virginia.

Principal Investigators:

Pratt, L.; Agne-Traub, C.E.; Stewart, S., et al.

Objective:

To (1) establish baseline data and competency levels for health curriculum development; (2) assess relationship between health behavior and cardiovascular knowledge; and (3) validate the National Examination of Cardiovascular Knowledge (NECK), a norm-referenced exam developed by the national headquarters of the AMA.

Methods or Approach:
Virginia was geographically divided into five regions with a state task force coordinator within each region. In the fall of 1983, 534 entering college freshmen in five geographically distributed universities were administered the NECK and in the spring of 1984, 4,917 10th and 12th grade students were given the NECK. The high school sample included rural and urban schools with random selection of counties and cities. The total sample was 65 percent white, 28 percent black, and 7 percent other; 47 percent males and 52 percent females. Students also answered demographic questions to reflect health behaviors. Health professionals assessed each item of the NECK to establish criteria for evaluating results.

Results to Date:
Data showed that 71 percent of college students, 68 percent of 12th graders, and 71 percent of 10th graders were never smokers. Of those who had started smoking, 55 percent of college students, 35 percent of 12th graders, and 46 percent of 10th graders stated they had quit smoking.

Future Plans:
Assessment of cardiovascular knowledge will be continued at the elementary school level (grades two and five) during the spring of 1985.

Project Dates:
May 1983–December 1985.

Financial Support:
Virginia Commonwealth University; AHA, Virginia.

1513. VIRGINIA COMMONWEALTH UNIVERSITY, 800 West Franklin Street, Richmond, Virginia 23284.

Project Title:
Cognitive Orientation and Smoking Behavior: The Construction of the Smoking and Health Questionnaire.

Principal Investigators:
Riebsame, W.; Tipton, R.

Objective:
To construct a smoking and health questionnaire with a self-report scale to determine cognitive orientation.

Methods or Approach:
Ideas from Kreitler and Kreitler's theory of cognitive orientation and behavior (1976) were used to guide construction of self-report rating scale. The conceptual framework of four belief types (self beliefs, general beliefs, norm belief, and goal beliefs) was used to write items. The resulting questionnaire was found to have sound psychometric properties with high levels of inter-item consistency within each belief subscale, test–retest reliability, and factorial stability. Meaningful utility was examined by obtaining concurrent validity estimates based on response patterns of smokers, ex-smokers, and nonsmokers.

Results to Date:
Analyses indicate that the questionnaire was able to significantly discriminate between health beliefs of smokers, ex-smokers, and nonsmokers. Length of smoking habit and number of cigarettes smoked/day were also significantly related to subjects' questionnaire responses.

Future Plans:
Questionnaires will be used as a dependent measure in a smoking cessation project utilizing a cognitive treatment approach.

Project Dates:
June 1984–March 1985.

Financial Support:
Virginia Commonwealth University.

1514. VIRGINIA COMMONWEALTH UNIVERSITY, Department of Pharmacology, Box 613, Richmond, Virginia 23284.

Project Title:
Control Sites of Nicotine: Involvement of Cholinergic and/or Noncholinergic Receptors.

Principal Investigator:
Rosecrans, J.A.

Objective:
To determine specific sites of nicotine action; establish whether sites are cholinergic or noncholinergic.

Methods or Approach:
Rats are trained to discriminate between nicotine and saline using a two-lever operant procedure. After rats are trained, cannulae are permanently implanted into a variety of brain areas to determine doses at which nicotine given peripherally (200 μg/kg), into a given site, will generalize. Studies are carried out with a variety of cholinergic agonists and antagonists.

Results to Date:
Two brain areas (hippocampus and reticular formation) appear to be important sites at which nicotine acts. Dopamine neurons may be indirectly involved in generalization of nicotine at the hippocampus. Other studies using physostigmine peripherally have failed to show that the nicotine cue is mediated via acetylcholine. However, arecoline appears to act at receptors innervated by acetylcholine.

Washington

1515. BATTELLE, PACIFIC NORTHWEST LABORATORIES, P.O. Box 999, Richland, Washington 99352.

Project Title:
Cigarette Smoke and Plutonium.

Principal Investigator:
Filipy, R.E.

Objective:
To (1) determine the influence of chronic exposure to cigarette smoke on the retention and distribution of inhaled insoluble plutonium particles in the respiratory tracts of laboratory rats and beagle dogs; (2) determine effect of cigarette smoke and plutonium on tracheal and bronchial mucosa; and (3) use animal data to determine whether or not human smokers are at greater risk of plutonium-induced respiratory tract cancer than nonsmokers.

Methods or Approach:
Rats and beagle dogs were exposed to cigarette smoke or sham-exposed for at least 7 months before exposure to a $^{239}PuO_2$ aerosol. Smoke and sham exposures were resumed after plutonium inhalation, and animals were subjected to periodic whole-body counting (17 keV x rays) to determine clearance of plutonium from respiratory tracts. Plutonium distribution in respiratory tracts was also measured with quantitative liquid

photographic emulsion autoradiography (rats) and with track-etch plutonium detection techniques (dogs).

Results to Date:

On the basis of whole-body counts, rats and dogs exposed to cigarette smoke cleared $^{239}PuO_2$ from respiratory tracts more slowly than animals not exposed to smoke. Rats cleared inhaled plutonium from lungs more rapidly than dogs, and young dogs (2 to 3 years old) had more rapid clearance rates than old dogs (10 to 12 years old). Plutonium particles were detected on inner surfaces of pulmonary airways by autoradiography. Smoke-exposed rats had less plutonium at these sites than sham-exposed rats 6 weeks after plutonium inhalation, attributed to a diminished mucociliary clearance at time of death. Numerous plutonium particles were detected in large bronchi of dogs up to 400 days after exposure, and many of the particles were determined to be within or beneath the bronchial mucosa, although a smoke effect was not apparent.

Future Plans:

Future plans include (1) investigation of methods for quantitation of autoradiographs made from bronchial mucosal preparations and (2) determination of epithelial cells at risk from radioactive emissions of plutonium retained within or below the bronchial mucosa of both rats and dogs. This will include enumeration of the types of cells present in epithelia and of mitotic responses of cells to radiation-induced injury.

Project Dates:

October 1977–continuing.

Financial Support:

DOE (E45-1-1830).

1516. FRED HUTCHINSON CANCER RESEARCH CENTER, 1124 Columbia Street, Seattle, Washington 98104.

Project Title:

Hutchinson Smoking Prevention Project (1984-).

Principal Investigators:

Peterson, A.V., Jr.; Nickerson, C.J.; Day, R.W., et al.

Objective:

To implement a multi-year sequential smoking prevention curriculum in selected high school feeder systems in the State of Washington; evaluate longitudinally the short- and long-term impact on actual smoking prevalence.

Methods or Approach:

A comprehensive smoking prevention curriculum will be developed from Project CHOICE by incorporating smoking prevention components adapted from existing smoking prevention curriculum used elsewhere. The program will be implemented by regular teachers in grades 3 through 10. Followup of third graders in years 1 and 2 will constitute the two consecutive study cohorts that will be followed for up to 14 years (2 years past high school). Actual smoking prevalence, as determined by self-report questionnaire, will also be biochemically validated (saliva cotinine). Data collection is designed to be simple, short, interesting to students, and infrequent. Students will be randomly assigned to the smoking prevention curriculum or control intervention. Approximately 40 geographically and demographically diverse high school feeder systems will be covered.

Results to Date:

Project is in a preliminary phase.

Project Dates:

August 1984–July 1989.

Financial Support:

NCI.

1517. FRED HUTCHINSON CANCER RESEARCH CENTER, SWEDISH HOSPITAL TUMOR INSTITUTE, 1309 Summit, Seattle, Washington 98104.

Project Title:

Chemoprevention of Lung Cancer With Retinol/Beta-Carotene.

Principal Investigator:

Goodman, G.E.

Objective:

To (1) assess the toxicity of long-term treatment with retinol and/or beta-carotene; (2) determine and compare the incidence of lung cancer in a high-risk population treated with retinol and/or beta-carotene; and (3) prospectively correlate plasma retinol and beta-carotene concentrations with subsequent development of cancer.

Methods or Approach:

The pilot project will determine the feasibility, compliance, and side effects of treating subjects at high risk for developing lung cancer with beta-carotene and/or retinol. The study population will consist of 230 male and female subjects with at least 20 pack-years of smoking (current smokers or those with less than 6 years of abstinence prior to enrollment). Patients, aged 50 to 67 years, will be randomized to (1) placebo, (2) retinol 25,000 units/day, p.o., (3) beta-carotene 30 mg/day, p.o., or (4) retinol and beta-carotene at the doses described. Followup will be every 2 months for 2 years. The treatment that is best tolerated will be utilized for a double-blind randomized placebo trial to determine the efficacy of the selected agent in decreasing the incidence of lung cancer in the high-risk population.

Results to Date:

The trial is in the startup phase. Protocols, forms, and questionnaires have been finalized, and drug and placebo procurement is proceeding. A sample of the target population has been screened for eligibility and compliance. Inquiry letters were sent to 1,000 households, resulting in 132 eligible subjects willing to participate. Letters to all potential participants will be sent in early 1985.

Future Plans:

It is anticipated that the pilot project will be completed by the end of 1986.

Project Dates:

July 1982–July 1986.

Financial Support:

NCI (1P50CA34847-01).

1518. FRED HUTCHINSON CANCER RESEARCH CENTER, 1124 Columbia Street, Seattle, Washington 98104.

Project Title:

Formaldehyde as Risk Factor for Nasal Cancer.

Principal Investigators:

Daling, J.R.; Vaughan, T.L.

Objective:

To determine if occupational and residential exposure to formaldehyde is associated with cancers of the nose, sinuses, and pharynx.

Methods or Approach:

The population-based case–control study will identify all persons aged 20 to 74 newly diagnosed with nasal, sinus, or pharyngeal cancer in 13 counties of western Washington via the SEER-based Cancer Surveillance System. Controls are selected from the general population through random-digit dialing. Telephone interviews inquire about smoking habits and occupational and residential histories.

Results to Date:
Results are not yet available.

Project Dates:
December 1982–October 1985.

Financial Support:
JRB Associates, Virginia.

1519. FRED HUTCHINSON CANCER RESEARCH CENTER, 1124 Columbia Street, Seattle, Washington 98104.

Project Title:
Hutchinson Smoking Prevention Project (HSPP).

Principal Investigator:
Peterson, A.V., Jr.

Objective:
To (1) determine whether implementation of a realistic multicomponent multiyear school-based smoking prevention intervention reduces smoking prevalence in junior high school students; (2) determine extent to which nonsmoking is maintained through and beyond high school; and (3) evaluate intervention process, including teacher training, program monitoring, teacher feedback, curriculum modification, and basic curriculum.

Methods or Approach:
Methodology of randomized controlled clinical trials will be adapted for the study, with special attention to problems of contamination and attrition inherent in prevention followup studies. The study population will be approximately 8,000 students in 40 geographically and demographically diverse high school feeder systems in the State of Washington. A feeder system consists of all elementary and junior high schools feeding into a senior high school. The curriculum will be sustained throughout the entire period of adolescent smoking onset, and will include early preparatory components starting in the third grade. Smoking behavior endpoints will be obtained when the initial 3rd grade cohorts reach the 5th, 7th, 9th, and 12th grades, and 2 years after high school.

Results to Date:
The prerandomization smoking survey for the first wave of participating school districts was completed in February 1985. Randomization and third grade curriculum intervention is planned for spring 1985.

Project Dates:
September 1984–August 1994.

Financial Support:
NCI (1R01CA38269-01).

1520. FRED HUTCHINSON CANCER RESEARCH CENTER, 1124 Columbia Street, Seattle, Washington 98104.

Project Title:
Alcohol and Cancers of the Mouth, Larynx, and Esophagus.

Principal Investigators:
Thomas, D.B.; Vaughan, T.L.; Davis, S.

Objective:
To (1) elucidate epidemiology of cancers of the mouth, larynx, and esophagus, with emphasis on role of alcohol; (2) examine risks associated with smoking and chewing tobacco, dental hygiene, occupation, and diet; and (3) determine independent effects of various trace elements, including selenium, using tissue samples (toenails) to yield prediagnosis measurements of micronutrient status.

Methods or Approach:
The population-based case–control study is following all persons 20 to 74 years of age diagnosed with laryngeal, esophageal, or oral cancer in King, Pierce, and Snohomish Counties in western Washington, identified through the SEER-based Cancer Surveillance System. Eligible cases (diagnosed between September 1983 and February 1987) are contacted for possible interview. Controls are randomly selected using random-digit-dialing techniques, and matched to oral cases by age and sex. Data concerning intake of specific foods are obtained by self-administered questionnaire. Information about prior use of alcohol and tobacco, dental health, occupation, medical history, and background data are obtained during a personal interview. Subjects also donate a clipping from each toenail for trace element analysis (neutron activation analysis). Further dental information is sought from current and past dentists.

Results to Date:
Results are not yet available.

Project Dates:
August 1983–February 1988.

Financial Support:
NCI (CA 30022-02).

1521. STATE OF WASHINGTON, Department of Social and Health Services, Health Data Unit, Mail Stop ET-14, Olympia, Washington 98504.

Project Title:
Lung Cancer Deaths Among Washington State Women.

Principal Investigator:
Starzyk, P.M.

Objective:
To examine patterns of lung cancer deaths among women, compared with deaths from other types of cancer and with lung cancer deaths among men.

Methods or Approach:
Death certificates for deaths registered with the State of Washington from 1968 to 1982 will be analyzed.

Results to Date:
By 1980, lung cancer death rates for women had surpassed death rates for breast cancer. Comparing current female lung cancer mortality rates with male rates 25 years earlier revealed similar patterns, indicating that smoking is involved in female lung cancer mortality. Lung cancer death rates for women have only recently begun to rise, because women took up smoking in large numbers about 25 years later than men.

Future Plans:
Monitoring of lung cancer incidence in Washington State women will continue.

Project Dates:
January 1983–completed.

Financial Support:
State of Washington.

Reference:
Starzyk, P.M. "Lung Cancer Deaths Among Washington Women." *Washington Morbidity Report* 1(1):1-4, January-February 1984.

1522. UNIVERSITY OF WASHINGTON, SCHOOL OF MEDICINE, Department of Pathology, 500 17th Avenue, Seattle, Washington 98195.

Project Title:
Mechanisms of Acute Vascular Reaction to Injury.

Principal Investigators:
Benditt, E.P.; Juchau, M.R.; Schwartz, S.M., et al.
Objective:
To study the response of cardiac vessel walls to injury.
Methods or Approach:
Mutagens in the urine will be studied using the Ames test. Studies of blood using the Ames test, as well as chemical tests and the measurement of sister chromatid exchanges, will be used as an indicator of exposure to cigarette smoke and other genotoxic substances. In addition functional and growth properties and response to injuries of endothelium, intimal and medial smooth muscle cells, and myocardial cells are being investigated in vivo and in vitro by ultrastructural, chemical, and cell culture analysis. The chemical structure and production of basement membrane in vessels and its role in repair of myocardial cells after local cardiac injury are being investigated. Source and functions of amyloid protein AA are also under investigation. A new way of viewing risk factors in atherosclerosis is being explored. The presence of mutagens derived from the environment (e.g., cigarette smoke) or from endogenous cholesterol in human lipoproteins is being sought. Mast cell interactions with lipids and lipoproteins and the relationship to heparin are also being studied. The role of mixed-function oxygenases in metabolism of promutagens to mutagens or cytotoxic agents by the artery wall is being investigated. The possible ways by which mutagens (extrinsic or intrinsic) may induce the cell population of atherosclerotic plaques to be monoclonal are under investigation. How hypertension and its chemical mediators affect the artery wall and may augment rates of atherosclerosis are also being investigated.
Results to Date:
The responses of three short-term mutagenesis assays (the Ames assay in mammalian cells (V-79); the sister chromatid exchange (SCE) rate alteration; and the cell mutagenesis (ouabain resistance) assay) to a number of known mutagens (N-methyl-N-nitroso-guanidine, benzo(*a*)pyrene, and cigarette smoke condensate (CSC) from the 2R1 test cigarette) were compared. All three assays showed a positive mutagenic response to the pure substances under the appropriate set of experimental conditions; the strength of the response to a particular pure mutagenic substance varied with the assay. However, CSC, a complex mixture, behaved differently in each of the assay systems. Using the Ames assay (with TA-1538), CSC was toxic to bacteria; with the addition of metabolic activator, however, CSC exhibited a linear dose–response and was scored as a strong positive mutagen. CSC was found to have a weak effect on SCE rate without metabolic activation; at higher concentration, CSC was toxic to cells without metabolic activation. CSC did not yield significant increases in mutation rates with V-79 cells and ouabain resistance. Thus, mutagenicity of a complex mixture, CSC, was found to be strongly test-dependent when a comparison of these popular short-term mutagenesis assays was conducted.
Project Dates:
March 1978–1982.
Financial Support:
NHLBI (P01-HL-03174-24).

1523. UNIVERSITY OF WASHINGTON, 1107 45th Street, NE., Seattle, Washington 98105.

Project Title:
Coordinating Center for Collaborative Studies in Coronary Artery Surgery.

Principal Investigator:
Davis, K.
Objective:
To determine in which subsets of patients coronary artery bypass surgery prolongs life.
Methods or Approach:
The collaborative clinical trial includes 15 clinical sites as well as the Coordinating Center and Project Personnel from the National Heart, Lung, and Blood Institute (NHLBI). A randomized trial component of 780 patients and a registry consisting of all 24,959 patients studied angiographically for suspected coronary artery disease are located at the clinical sites. Although the emphasis is on survival and the relationship to the surgical technique, part of the baseline data collected involves the smoking history of the individual studied.
Results to Date:
Smoking was found to be a definite risk factor for coronary artery disease, especially in younger persons, among those studied angiographically. Continued smoking among individuals with coronary artery disease may increase mortality by as much as 30 percent.
Project Dates:
May 1973–1986.
Financial Support:
NHLBI (N01-HV-32973).
References:
(1) Vliestra, R.E.; Frye, R.L.; Kronmal, R.A., et al. "Risk Factors and Coronary Artery Disease: A Report From the Coronary Artery Surgery Study (CASS)." *Circulation* 62(2):254-261, August 1980. (2) Vliestra, R.E., et al. "Stopping Smoking Improves Survival in Patients with Angiographically Proven Coronary Artery Disease." *American Journal of Cardiology* 49(part 2):984, 1982 (Abstract).

1524. UNIVERSITY OF WASHINGTON, COLLEGE OF EDUCATION, 309 Miller Hall, DQ-12, Seattle, Washington 98195.

Project Title:
Effects of the School Health Curriculum Project (SHCP) on Health Knowledge, Attitudes, and Behavior of Students.

Principal Investigator:
Andrews, R.L.
Objective:
To (1) determine effects of the Growing Healthy Curriculum Project on schoolchildren's knowledge about health, smoking, and body systems; (2) determine effects of the Growing Healthy Curriculum Project on children's attitudes about smoking and good health practices; (3) determine effects on internal locus of control and independence in decisionmaking; and (4) determine program participation effects on family health practices.
Methods or Approach:
The longitudinal study involves 376 children who entered kindergarten in 1977 and will complete seventh grade in 1985. Sixteen elementary schools in three suburban school districts participated; 188 children in one district were the experimental group, and 376 children in similar districts were the control groups. Districts are similar in socioeconomic status, ethnic composition, achievement stanine distribution, and average level of achievement. Students in the experimental group are treated by classroom groups and rotated through the four learning stations in groups of five to six children. The approach used consists of specific health content that presents the body as a network of systems that require cultivation and care. The learning/teaching method emphasizes small group learning,

peer teaching, experimental activities, and teachers trained in health education and experiential learning. Each child received an average of ten 40-minute health experiences at each grade level from kindergarten to third grade. The control group received the standard elementary school curriculum, alone or in conjunction with the SHCP in fourth, fifth, and sixth grades. Cognitive and affective pretests were administered in October 1977, and posttests in June 1984, to both experimental and control groups. In addition, a survey designed to assess student experimentation, exposure, and future expectancy to engage in substance use and abuse was administered as a posttest in June 1984. Analysis of covariance was used to assess treatment effect on cognitive and affective posttest scores, controlling for pretest scores. Chi-square tests were used to test the significance of differences on the various items from the student survey.

Results to Date:

Children who were pretested in September 1977 have participated in 7 years of the 12-year project. Experimental group children attained significantly higher cognitive ($p=0.01$) and affective ($p=0.001$) posttest scores than students in at least one of the control groups. There were significant variations between the experimental group and control group in the number of students who reported they experimented with or used tobacco, alcohol, or drugs on a regular basis. There were significant variations in the percentage of students who had tried smoking ($p<0.05$). Lower frequencies favored the experimental group. There were significant variations between the experimental and control groups in the number of students who reported that their friends had experimented with alcohol ($p=0.03$), who reported drinking alcohol on a regular basis ($p=0.002$); and future expectancy to drink or most or many friends who drink ($p=0.001$, $p=0.01$), respectively. A significant variation was found for personal experimentation (have tried alcohol). There were significant variations between the experimental and control groups on experience, exposure, and future expectancy to engage in marijuana and/or other dangerous drug use.

Future Plans:

In June 1985, the children will be tested at the end of seventh grade for differences in (1) cognitive and affective levels; (2) experimentation, engagement, and future expectancy to smoke, drink alcohol, and use drugs; and (3) spin-off effects on families' general health practices and cessation of smoking. In addition, a longitudinal followup of participants is planned for 9th and 11th grades.

Project Dates:

September 1977–June 1990.

Financial Support:

University of Washington; ALA.

1525. UNIVERSITY OF WASHINGTON, 3937 15th Avenue, NE., Seattle, Washington 98105.

Project Title:

Lactation–Diet, Drinking, Smoking and Infant Growth (Human).

Principal Investigator:

Little, R.E.

Objective:

To investigate patterns of maternal diet, alcohol, and tobacco use during lactation and to study the relationship of these patterns to infant growth and development.

Methods or Approach:

A pilot study of 100 women will be conducted to test validity, reliability, and feasibility of methods and instruments. Later, a sample of 200 currently lactating women and 200 women who have never lactated will be drawn. Maternal nutrient intake, food choices, cravings and aversions, and alcohol and tobacco use will be measured 1, 2, and 3 months postpartum. Differences between lactating and nonlactating women will be compared, and relationships among the variables will be explored. One-year followup will be used to obtain current estimates of both maternal and infant nutrient intake to determine how the two are related. Assessment of the relationship of alcohol and tobacco use during lactation to infant development will be explored in a sample, stratified on frequency of use both during and after pregnancy, and on lactation status. Infants will be examined at 1 year to assess psychological and physical development. Infants of mothers who smoked or drank alcohol during lactation will be compared with infants whose mothers did not. If differences in growth and development exist, confounding variables will be examined to determine if they might account for the observed differences. Additional analyses will evaluate the role of environmental factors and the relative effects of prenatal and postnatal exposure.

Results to Date:

Project is in a preliminary phase.

Project Dates:

May 1982–May 1987.

Financial Support:

NICHD (HD 14689); University of Washington.

1526. UNIVERSITY OF WASHINGTON, Department of Pathology, SM-30, 500 17th Avenue, Seattle, Washington 98195.

Project Title:

Reaction to Injury.

Principal Investigator:

Benditt, E.P.

Objective:

To investigate factors in cigarette smoke that may contribute to development of atherosclerotic lesions.

Methods or Approach:

Biochemical measures will include enzyme analyses; morphological studies will include light microscopy, scanning electron microscopy, and transmission electron microscopy.

Results to Date:

Polynuclear aromatic hydrocarbons, including those present in tobacco smoke, are capable of exacerbating atherosclerotic lesions in avian species.

Future Plans:

Initiation and promotion studies will be conducted.

Project Dates:

March 1983–February 1988.

Financial Support:

NIH.

1527. UNIVERSITY OF WASHINGTON, Social Work Research, WJ-10, Seattle, Washington 98195.

Project Title:

Alcoholics and Cigarette Smoking.

Principal Investigators:

Bobo, J.K.; Schinke, S.P.; Gilchrist, L.D.

Objective:

To (1) compare demographics and substance abuse histories of recovering alcoholics who successfully quit smoking with those who unsuccessfully attempt cessation; (2) examine impact of smoking cessation efforts on maintenance of sobriety; and (3) suggest preferred cessation strategies for this subpopulation of smokers.

Methods or Approach:

Subjects recruited from the community were screened by telephone. The 77 adult men meeting preset criteria for alcohol and tobacco use histories also completed a 45-minute telephone interview that reviewed onset, intensity, and duration of alcohol and tobacco use. Smoking cessation attempts subsequent to the completion of inpatient alcohol treatment were thoroughly detailed. Finally, the strength of agreement with commonly endorsed perceptions on interrelationships between smoking and drinking was assessed. All subjects provided names and addresses of two individuals who were able, in general, to verify the respondent's self-reported alcohol and tobacco use experience.

Results to Date:

Preliminary data analysis is underway. The sample appears to be demographically representative and adequately balanced between those with successful and unsuccessful cessation attempts. Descriptive and correlational data will be reported when available.

Future Plans:

Data analysis may guide the development of an experimental smoking cessation program for the subpopulation of smokers and/or delineate areas needing more sophisticated study.

Project Dates:

March 1984–June 1985.

Financial Support:

ACS (IN-264).

1528. UNIVERSITY OF WASHINGTON, Department of Medicine RG-26, Seattle, Washington 98195.

Project Title:

Japanese American Community Diabetes Study.

Principal Investigator:

Fujimoto, W.Y.

Objective:

To examine the role of environmental and other factors, including psychosocial and cultural, in the cause and complications of diabetes mellitus in Japanese-American men in Seattle.

Methods or Approach:

Japanese-American men have a much greater prevalence of diabetes than similarly aged Japanese or Caucasian men. The roles of age, body fat storage, diet, use of alcohol and tobacco, physical activity, lifestyle, and social stress will be examined in relation to the development of type II (noninsulin dependent) diabetes, development of complications including eye, kidney, and nerve damage, and the occurrence of atherosclerosis. The study cohort consists of 250 Nisei men (born in the United States as children of immigrants who arrived prior to 1925). Information is gathered by (1) sociocultural interview (social history, lifestyle activities, social networks, stress and coping, community involvement); (2) health history and habits interview (health review, use of tobacco and alcohol, sleep, habitual physical activity); (3) clinical study (physical exam, fundoscopic exam, electrocardiogram, nerve conduction exam, assessment of peripheral arterial blood flow by Doppler, 75 g oral glucose tolerance test, plasma lipids and lipoproteins, creatinine clearance, urinary excretion of glucose and protein, bone density, pulmonary function, pattern of fat distribution as assessed by CT scan); (4) diet interview; and (5) anthropometry.

Results to Date:

Among a random sample of Nisei men and women in the Seattle area, 12 percent of men and 8 percent of women reported the presence of diabetes. During the first year, 74 Nisei men (age range 50 to 70 years) who believed they did not have diabetes participated in a 75 g oral glucose tolerance test; 45 percent had normal glucose tolerance, 42 percent had impaired glucose tolerance, and 13 percent had diabetes. Approximately 140 Nisei men have been studied to date. Preliminary data analysis has been completed on the first 75 participants (25 normal, 30 diabetic, 20 impaired). Although caloric intake was similar, men with diabetes consumed proportionally less carbohydrate and more fat daily than did normal men, while men with impaired glucose tolerance were intermediate. Although 80 percent of Nisei men have smoked cigarettes, only 13 percent currently smoke. This change was greatest for diabetic men (from 87 percent to 7 percent), least for men with impaired glucose tolerance (75 percent to 20 percent), and intermediate for normal men (76 percent to 16 percent). Over 40 percent had plasma cholesterol >250 mg/dL; no differences were found between groups. Diabetic men had a greater ratio of upper body to thigh subcutaneous fat areas and a greater amount of intra-abdominal fat than normal men. ECG evidence of ischemic heart disease was present in 20 percent of diabetic men and 8 percent of normal men. Retinopathy and renal impairment was extremely uncommon, as was peripheral arterial disease. Neuropathy was present in over half of diabetics.

Future Plans:

A collaborative study with investigators in Japan is planned that will include (1) samples of the general Japanese population and (2) residents who are first cousins to the Japanese-American subjects in Seattle. Ways to transfer and adapt the Seattle protocol for use in Japan will be determined.

Project Dates:

June 1983–May 1986.

Financial Support:

NIH (AM 31170).

1529. UNIVERSITY OF WASHINGTON, Department of Psychology, NI-25, Seattle, Washington 98195.

Project Title:

Relapse Prevention in Cigarette Smokers.

Principal Investigators:

Marlatt, G.A.; Gordon, J.R.; Curry, S.G.

Objective:

To provide in-depth, longitudinal analysis of factors associated with success or failure in a group of smokers who have quit smoking on their own; to assess relative effectiveness of a relapse prevention and traditional behavioral program for smoking cessation when programs are offered in both group and self-quit formats.

Methods or Approach:

In the study of unaided quitters, 153 smokers who planned to quit for New Year's 1981 were recruited from the general public and interviewed 1 month, 4 months, 1 year, and 2 years after their quit date. Information obtained included smoking status, demographics, smoking history, beliefs and expectancies, and descriptions of high risk for relapse situations. In the treatment study, two programs were developed: (1) relapse prevention (RP), which emphasized skill training and cognitive restructuring; and (2) traditional, absolute abstinence (AA), which emphasized aversive conditioning and contingency management. Programs were offered in group and correspondence formats. The 145 participants enrolled were randomly assigned to one of four treatment conditions. Followup data obtained at end of treatment and at 1 year posttreatment included smoking status, demographics, smoking history, self-efficacy, social support, outcome expectancies, attributions for success or failure outcomes, lifestyle balance, beliefs about cigarette smoking and smoking cessation treatment, and life stress.

Results to Date:
Only 75 percent of those who planned to quit on their own managed to do so for at least 24 hours. At 2 years, 18 percent of unaided quitters were not smoking. Employment status, income, and desire to quit were related to initial cessation; use of coping strategies and outcome expectancies were related to short-term abstinence; and prior quitting experience, outcome expectancies, and desire to quit were related to long-term abstinence. Results from the treatment outcome study are currently being analyzed. For participants who began treatment, no significant differences were found in smoking outcomes for the four treatment conditions. Compared with unaided quitters, significantly more treatment participants maintained abstinence for 1 year (37 percent vs. 18 percent). Among treatment participants who smoked one cigarette post-quit, those who attributed the cause of smoking to internal, stable, and global factors were more likely to resume regular smoking.

Future Plans:
The treatment program is currently being tested in a worksite smoking cessation study and plans are under way for using the program in an evaluation of treatment programs targeted at women with low socioeconomic status.

Project Dates:
June 1980–November 1984.

Financial Support:
NIDA (R01DA02572).

1530. UNIVERSITY OF WASHINGTON, SCHOOL OF PUBLIC HEALTH AND COMMUNITY MEDICINE, HANFORD ENVIRONMENTAL HEALTH FOUNDATION, FRED HUTCHINSON CANCER RESEARCH CENTER, Seattle, Washington 98195.

Project Title:
Worksite Smoking Cessation and Relapse Prevention.

Principal Investigators:
Omenn, G.S.; Breitenstein, B.D.; Michnich, M., et al.

Objective:
To (1) adapt recently developed smoking cessation and relapse prevention programs for application in an industrial setting; (2) train key occupational health care personnel in smoking cessation and relapse prevention techniques; (3) develop baseline profiles on smoking behaviors within the defined population of employees at the Hanford Reservation; (4) systematically test the relative effectiveness of specified smoking cessation strategies and relapse prevention techniques; and (5) incorporate individual smoking cessation data into the ongoing long-term epidemiologic study of morbidity and mortality at Hanford.

Methods or Approach:
The project is a joint effort of the Hanford Environmental Health Foundation, an organization providing occupational hygiene, medical, psychological, and research services to 13,000 Hanford workers, the Fred Hutchinson Cancer Research Center, and the University of Washington. It consists of three stages: baseline data collection and material/resource development in year 1, intervention in year 2, and evaluation during year 3. Baseline data are being used to identify smokers who are interested in receiving information on smoking cessation. Smokers will be randomly assigned to (1) a group-oriented multiple component program, (2) a group-oriented relapse prevention program, (3) a self-quit multiple component program, (4) a self-quit relapse prevention program, or (5) a control group. Baseline data are collected and quarterly followups will be conducted on each participant for 12 months. Relative effectiveness of the programs will be examined.

Results to Date:
During stage one, two existing intervention strategies were adapted for large-scale applications in work settings. Key Hanford personnel were trained in intervention techniques and an employee survey was conducted to profile smoking behaviors and attitudes within the Hanford work population. The first wave (pilot) of interventions was conducted during October and November 1984. Self-identified smokers who were interested in receiving information on smoking cessation were randomized into treatment groups and invited to participate. Participation rates were relatively low, but most of those who did participate were successful in reducing or quitting smoking. The pilot wave led to development of additional strategies to increase participation and some revisions of the protocol.

Future Plans:
Additional intervention waves will be conducted until all 1,400 smokers have been served. Subjects will be followed to ascertain relapse rates of various programs, and questionnaire followups will be verified by a biochemical marker at 12 months. End products, after data analysis, will include training materials, teaching aids, self-assessment information to be applied to other worksites, and plans for a continuing program at this worksite.

Project Dates:
July 1983–June 1986.

Financial Support:
NCI (R01P50CA34847).

1531. UNIVERSITY OF WASHINGTON, SCHOOL OF PUBLIC HEALTH AND COMMUNITY MEDICINE, Seattle, Washington 98195. FRED HUTCHINSON CANCER RESEARCH CENTER, 1124 Columbia Street, Seattle, Washington 98104.

Project Title:
Cancer Prevention With Retinol and Beta Carotene in Persons With Asbestos Related Lung Disease.

Principal Investigator:
Omenn, G.S.

Objective:
To (1) determine efficacy of chemoprevention with daily oral retinol/beta-carotene in patients at high risk for bronchogenic carcinoma; (2) determine efficacy of chemoprevention with daily oral retinol/beta-carotene in patients at high risk for malignant mesotheliomas; (3) assess toxicity and safety of the chemoprevention regimen; and (4) demonstrate feasibility and usefulness of recruiting subjects with specific occupational exposure through employment and worker's compensation systems.

Methods or Approach:
Approximately 2,500 subjects with asbestos-related lung disease will be stratified by smoking status and by year since first exposure to asbestos (<40 or ≥ 40 years). Within strata, subjects will be randomly assigned to treatment (25,000 U retinol and 15 mg beta-carotene/day) or placebo. When participants are recruited for the 5-year study, smokers will be advised that the only known way in which their risk of bronchogenic cancer may be decreased is to stop smoking. This information will be included in the informal consent, and again in interviews with the clinical trial nurse.

Results to Date:
Recruitment will begin in January 1985.
Future Plans:
Long-term objectives would include broadly based population studies if this intervention appears to be effective.
Project Dates:
July 1983-June 1988.
Financial Support:
NCI (1P50CA34847-01).

1532. UNIVERSITY OF WASHINGTON, SCHOOL OF SOCIAL WORK, JH-30, Seattle, Washington 98195.

Project Title:
Smoking Prevention Training for High-Risk Youth.

Principal Investigators:
Schinke, S.P.; Gilchrist, L.D.
Objective:
To (1) evaluate methods of preventing tobacco use by persons from rural, blue-collar, low-income, nonwhite, or single-parent backgrounds; (2) evaluate use of booster sessions to maintain effects of tobacco use prevention; (3) validate an index to assess future tobacco use; and (4) measure test reactivity in tobacco use prevention research.
Methods or Approach:
Two panels of sixth grade students will be screened for risk of future tobacco use. Forty-eight schools, each with enrollments of at least 50 percent high-risk students, will be divided into four conditions. Estimated total number of students is 6,048 (756 per condition per panel). Two experimental conditions will receive an 18-session curriculum covering information, problem solving, self-instruction, communication skills, and media analysis. One experimental condition will receive semiannual booster sessions when subjects are in seventh, eighth, and ninth grade. The independent variable will be monitored with observational data, subject feedback, and session summaries. The other two conditions will be untrained controls: one will be tested only at the beginning and end of the study; the other (and both experimental conditions) will be tested annually. Outcome measures will cover demographic information, self-reports of tobacco use, self-reported health behavior, self-reinforcement, problem solving, interpersonal coping, assertiveness, social networks, and self-efficacy. Assays of saliva thiocyanate will be used to confirm reports of tobacco use. Followup will measure contagion relative to prevention curricula. Results will be analyzed for effects of gender, demographic characteristics, prevention curriculum, and booster sessions. Multivariate procedures will prospectively test an index to predict youths' future tobacco use and nonuse.
Results to Date:
Preliminary outcome data will be available in June 1986.
Future Plans:
Prospective validation of a screening instrument for assessing risk of becoming a smoker will be completed by December 1989.
Project Dates:
January 1985–December 1989.
Financial Support:
NCI (2R01CA29640).

1533. UNIVERSITY OF WASHINGTON, CHILD DEVELOPMENT AND MENTAL RETARDATION CENTER, Seattle, Washington 98195.

Project Title:
Smoking Prevention Training for Youth.

Principal Investigators:
Schinke, S.P.; Gilchrist, L.D.
Objective:
To develop, field test, and evaluate a self-control skills training curriculum for prevention of cigarette smoking among adolescents.
Methods or Approach:
After pretesting, 741 male and female fifth and sixth grade students were randomly assigned (by school) to experimental, placebo, or control condition. The experimental group curriculum included health information, problem-solving techniques, self-instruction procedures, and communication skills. These groups were compared with placebo groups that received only health information and with assessment-only control groups. Instruments to assess prevention training included questionnaires on experiences, attitudes, intentions, and knowledge of cigarette smoking; problem-solving and decisionmaking measure; refusal skills measure; inventory of covert self-statements; questionnaires about cigarette use; and assays for saliva thiocyanate. Subjective satisfaction with the program was reported by sixth grade participants, their teachers, and school administrators. Longitudinal followup assessed persistence of smoking prevention training.
Results to Date:
Using pretests as covariates, posttest condition differences favoring self-control training were found for refusal skills ($p<0.01$), self-instruction skills ($p<0.05$), self-praise skills ($p<0.01$), and compliance with peer pressure ($p<0.01$). Followup indicated a gradual shift in relative percentages of regular smokers (defined as those who reported smoking one or more cigarettes in the last 7 days). At pretest, 4 percent of the experimental group, 3.2 percent of the placebo group, and 3.9 percent of the control group were regular smokers. Posttest measures indicated a modest decrease in the experimental group and a slight increase in the placebo and control groups (3.8 percent, 5.0 percent, and 4.5 percent, respectively). At 15-month followup, differences were more pronounced: 5.8 percent in the experimental group, 9.2 percent in the placebo group, and 8.3 percent in the control group.
Future Plans:
To further evaluate effectiveness, the curriculum will be implemented with sixth graders at high risk for becoming adult smokers. Students will be paired by site with controls (no treatment) and followed through the tenth grade.
Project Dates:
April 1981–July 1984.
Financial Support:
NCI (R18CA29640).

1534. VETERANS ADMINISTRATION MEDICAL CENTER, 4435 Beacon Avenue, S., Seattle, Washington 98174.

Project Title:
MR II Atherosclerosis in Uremia.

Principal Investigator:
Sherrard, D.
Objective:
To clarify the causes and significance of accelerated atherosclerosis in patients with chronic renal failure.
Methods or Approach:
Prospective epidemiologic assessment of known risk factors and clinical-biochemical studies characterizing the lipid disorder have been carried out.
Results to Date:
Cardiovascular disease is a consequence, at least in part, of

high blood pressure, smoking, and elevated triglyceride levels. It has been shown that elevated triglyceride levels can be a consequence of a variety of disturbances in uremia that inhibit lipoprotein lipase. Also, clofibrate can be used safely, at very low doses, to lower triglyceride levels in these patients. More recent findings suggest an interaction of drugs, such as androgens, beta blockers, and cimetidine, and abnormal calcium metabolism with the lipid disorder. In addition, it has been demonstrated that lipid levels are constant over a prolonged time period (i.e., 5 years); thus, patients assigned to various therapeutic or "risk" groups based on lipid levels at one point in time will remain at the same lipid level if untreated.

Financial Support:
VA.

1535. VETERANS ADMINISTRATION MEDICAL CENTER, 4435 Beacon Avenue, S., Seattle, Washington 98108.

Project Title:
The Effect of Stressful Life Events Upon the Smoking Cessation Process.

Principal Investigators:
Bailey, G.J.; Belcher, D.W.

Objective:
To (1) determine the frequency and distribution of stressful life events among patients attending a health promotion clinic; (2) determine whether these stressful life events affect the probability of success for a participant in smoking cessation program; (3) assess whether the presence of depression or concurrent use of alcohol modifies the effects of these stressful life events on program success; and (4) develop a statistical model to predict probable success in a smoking cessation program for Veterans Administration outpatients.

Methods or Approach:
Stress was assessed along with alcohol use, depression, and other health variables before smokers began a cessation program. Subsequent smoking status was determined by followup interviews with individuals or significant others by telephone. The Sarason Life Experiences Survey (LES) was used to allow patients to create the impact of stressful life events on themselves. Zung depression scores, alcohol SMAST scores, and other related variables were also determined before beginning the cessation program. Smoking status was determined at 4 weeks and 4 months, and will be corroborated at 1 year with spirometry and carbon monoxide tests.

Results to Date:
A total of 144 patients satisfactorily completed the LES stress questionnaire. Sixty-one were present smokers, 52 of whom also attended the smoking cessation program. Eleven smokers had quit at the 4-month followup, one died, and three have been lost to followup. Quitters reported more stress than those who were still smoking 4 months after followup, but this difference was not significant after adjustment for age. The most important predictors of smoking cessation were age (those aged 50 to 59 were more likely to quit than either younger or older subjects), alcohol use (present users were least likely to quit, followed by past users and then never users), and previous quit attempts (the more often a patient had tried to quit in the past, the more likely he was to succeed this time).

Financial Support:
VA.

1536. VETERANS ADMINISTRATION MEDICAL CENTER, 4435 Beacon Avenue, S., Seattle, Washington 98108.

Project Title:
Disease Prevention and Health Maintenance Program Trial.

Principal Investigators:
Belcher, D.W.; Inui, T.S.; Carter, W.B.

Objective:
To compare three innovative delivery models' impact upon preventive care services received by 1,200 Seattle Veterans Administration Medical Center (VA) service-connected outpatients over a 4-year period (September 1981–August 1985).

Methods or Approach:
After selecting a set of age- and sex-specific preventive care activities, a baseline audit (1978–1981) of 1,500 charts was conducted to determine the completeness of outpatient preventive care and to identify any patient group at greater risk of not receiving such care. Intervention models include a disease-screening clinic (staffed by a nurse practitioner) and two clinic-based strategies involving either special patient education materials (e.g., Pocket Guide) or clinician orientation to use of a chart flowsheet (screening guidelines). Annual chart audits are being analyzed across study groups and for selected patient and clinic variables.

Results to Date:
Overall, preproject preventive care is low: only one (blood pressure measurement) of the 16 recommended screening/counseling activities was documented in 25 percent or more of audited charts. Preliminary analysis shows that subjects allocated to the four study groups are comparable in age, principal clinic or care, prior Veterans Administration (VA) preventive care, use of tobacco and alcohol, and VA clinic visits/year. Age does not affect baseline receipt of preventive care services, but patients affiliated with surgical, psychiatric, and to some extent, medical subspecialty clinics were much less likely to receive preventive care than general medicine clinic attenders. Initial volunteerism rate (71 percent) and year 2 return rate (91 percent) for the screening clinic program was high, indicating patient interest in such care and satisfaction with the program. Information about screening yield, followup care, and direct costs has been developed. Preliminary data analysis after 1 year of patient and clinician education intervention models shows no significant increase in preventive care activities compared with baseline levels.

Future Plans:
Because patient activation and clinician reorientation involves fairly complex behavior, a longer time (i.e., 2 years) is needed to reach any conclusion regarding these low-cost clinic-based interventions. If a lack of impact persists through year 2, the two education groups will be combined as a more powerful strategy to attempt to reach outpatients who might not volunteer for a separate screening program.

Financial Support:
VA.

1537. VETERANS ADMINISTRATION MEDICAL CENTER, 4435 Beacon Avenue, S., Seattle, Washington 98108.

Project Title:
The Risk of Ulcerative Colitis in Relation to Use of Tobacco.

Principal Investigators:
Boyko, E.J.; Koepsell, T.D.; Perera, D.R.

Objective:
To examine whether use of tobacco, coffee, and alcohol influence the risk of developing ulcerative colitis.
Methods or Approach:
A case-control study will be performed at Group Health Cooperative of Puget Sound. Approximately 400 cases have been identified among Group Health enrollees using gastroenterology division index card files, computerized pharmacy information, and hospital discharge data and by direct mail contact with every Group Health physician. From among the cases, 225 will be selected randomly for inclusion in the study. An equal number of age- and sex-matched controls will be systematically selected from the current Group Health enrollment file. A telephone interview will be used to gather information on use of tobacco, coffee, and alcohol and on socioeconomic status. Data analysis will determine risk of ulcerative colitis in tobacco users as opposed to nonusers, while controlling for possible confounding factors not considered in previous studies, through use of stratified analysis and conditional logistic regression.
Results to Date:
Approximately 380 subjects must still be interviewed.
Project Dates:
February 1984–continuing.
Financial Support:
VA.

1538. VETERANS ADMINISTRATION MEDICAL CENTER, 4435 Beacon Avenue, S., Seattle, Washington 98108.

Project Title:
The Effect of Chronic Bronchitis on Lung Cells.

Principal Investigators:
Martin, T.R.; Springmeyer, S.; Raghu, G.
Objective:
To determine whether the presence of chronic bronchitis alters cell populations in bronchoalveolar lavage fluid recovered from the lung.
Methods or Approach:
Bronchopulmonary lavage was performed on 48 patients who underwent fiberoptic bronchoscopy for either hemoptysis or pulmonary mass lesions. Each patient was given a questionnaire before bronchoscopy to determine the presence or absence of chronic bronchitis and the amount of cigarette use. The lavage procedure was performed in a subsegment of the right middle lobe or lingula. Five separate aliquots of saline were instilled, and each aliquot was analyzed for cell populations, cell viability, total protein, IgG, and IgA.
Results to Date:
The mean percentage of polymorphonuclear leukocytes (PMN) in the pooled lavage sample from each patient was 11.19±3.7 percent; however 17/48 (35.4 percent) of patients had over 10 percent PMN in the pooled sample (mean 37± 6 percent; range 10 to 87.5 percent). Lavage PMN correlated moderately with decreasing forced expiratory volume in 1 sec ($r=0.51$, $p<0.01$), but not with current tobacco use or the presence or absence of chronic bronchitis. Therefore, increased PMN can be found in lavage fluid from patients with chronic airflow obstruction regardless of cessation of smoking and the absence of clinically evident bronchitis. In diffuse lung disease, lavage PMN indicate the presence of a neutrophilic alveolitis that may contribute to lung destruction. However, when chronic airflow obstruction coexists with diffuse lung disease, the presence of PMN in lavage fluid may not be an accurate reflection of the alveolitis component of the interstitial lung disease.
Financial Support:
VA.

1539. WASHINGTON DEPARTMENT OF SOCIAL AND HEALTH SERVICES/EPIDEMIOLOGY, 1409 Smith Tower, Mail Stop B17-9, Seattle, Washington 98104.

Project Title:
Passive Smoking: Myth or Reality?

Principal Investigators:
Frost, F.; Hafer, R.F.
Objective:
To provide public education about passive smoking through distribution of a pamphlet to health providers.
Methods or Approach:
A review of literature on passive smoking and its health effects was made and a brief review article was produced for publication in the *Washington Morbidity Report*.
Results to Date:
There was enthusiastic public response to dissemination of the report.
Future Plans:
It is anticipated that the same or modified article will be published elsewhere, to reach other audiences.
Project Dates:
March 1984–June 1984.
Financial Support:
Washington State Department of Social and Health Services/Epidemiology.
Reference:
Hafer, R.F.; Frost, F. "Passive Smoking: Myth or Reality?" *Morbidity Report* 1(2):1-4, 1984.

1540. WASHINGTON STATE HEALTH LABS - EPIDEMIOLOGY, DEPARTMENT OF SOCIAL AND HEALTH SCIENCES, 1409 Smith Tower, Mail Stop B17-9, Seattle, Washington 98104.

Project Title:
Washington State Risk Control Survey.

Principal Investigator:
Hafer, F.
Objective:
To develop information for the executive branch of the State government to use in justifying programs and actions and to conduct an extensive assessment of the incidence and prevalence of morbidity and mortality by geographic area and demographic sectors of the State.
Methods or Approach:
A telephone survey will be conducted to assess public attitudes toward potential control strategies for the three leading contributors to preventable/premature morbidity and mortality: injuries, smoking, and alcohol consumption.
Results to Date:
Results are not yet available; the survey will be started in January 1985.
Future Plans:
It is anticipated that, over time, the entire State will be surveyed.
Project Dates:
August 1984–continuing.
Financial Support:
Washington State Health Labs.

1541. WASHINGTON STATE UNIVERSITY, SOCIAL RESEARCH CENTER, Wilson Hall, Pullman, Washington 99164.

Project Title:
Value Approach to Reducing and Preventing Smoking.

Principal Investigator:
Rokeach, M.
Objective:
To determine whether awareness of certain types of contradictions might be effective in arousing psychological states culminating in quitting, reducing, or deterring smoking.
Methods or Approach:
Making adolescents who say they want to quit, or who say they do not want to start smoking, aware of contradictions existing between (A) their own values, (B) their cognitions or perceptions of the values of smokers and nonsmokers (including ex-smokers), and (C) the actual values of smokers and nonsmokers is hypothesized to lead to arousal of affective states culminating in health-constructive values and in the reduction or deterrence of smoking. In the case of adolescents who already smoke and say they want to quit smoking, pointing to contradictions between (A) and (B), or between (A) and (C), or between (B) or (C) should lead to the arousal of dissatisfaction with their own values and their value images of smokers and nonsmokers, and thence to changing their values to better support nonsmoking. In the case of adolescents who do not yet smoke and say they want to continue to not smoke, it should lead either to the arousal of dissatisfaction with one's own values if they are discrepant with nonsmoking, or to the arousal of satisfaction with (and thus stabilization of) one's values if they already support nonsmoking. Surveys of recent high school graduates were undertaken to establish baseline data on target values (Rokeach Value Survey, 1967), smoking behaviors, and other influences on smoking. The value data were used to prepare three experimental video tapes which were shown to students of several experimentally assigned schools. Some students were also exposed to social support–social control for not smoking treatment conditions. Pretests, interventions, and four posttest measures spanning a year were taken to determine the effects of the experiment.
Results to Date:
Data collection has been completed and analysis in underway. Two papers have been presented at professional meetings, one paper has been published, and several manuscripts are in preparation.
Project Dates:
June 1980–1984.
Financial Support:
NIDA (DA02556).

1542. WASHINGTON STATE UNIVERSITY, Department of Sociology, Social Research Center, Pullman, Washington 99164.

Project Title:
Smoking and Youth: A Developmental Study.

Principal Investigators:
Mauss, A.L.; Hopkins, R.H.
Objective:
To test a general etiological model of onset of smoking in children, with special reference to pubescent years; assess usefulness of certain health education components in an intervention strategy aimed at "innoculating" them psychologically against substance use and abuse.
Methods or Approach:
Research is based on secondary analysis of data collected for an earlier health education project that focused on prevention of alcohol use and abuse in children that also contains information on smoking habits. Students in grades 4 through 12 responded to standardized tests or questionnaires administered at various intervals across a 3-year time span. Research has consisted of extensive discriminant analysis, with both longitudinal and cross-sectional subsamples, to identify variables most responsible for changes in smoking status across time. Work is also proceeding via the LISREL method on a more elaborate causal model of the changes. A satisfactory measurement model, but not a structural model, has been identified, and findings to date are based mainly on discriminant analysis.
Results to Date:
The most important predictors of change over time to increased cigarette smoking during junior high school years are (1) extent to which children perceive their peers to be substance users (especially alcohol); (2) extent to which one is influenced by peers as opposed to parents; and (3) extent to which one is not committed to conventional rules and activities. Secondary (but still important) predictors include satisfaction with school, knowledge about substances (especially alcohol in this data set), and inability to assign responsibility for problems. Some variations are found for sex and age, but in general the variations are not great. Sample sizes were too small to include ethnicity as a variable.
Project Dates:
February 1983–August 1985.
Financial Support:
NICHHD (1R01HD16198-01A1).

1543. DHHS, PHS, CDC, NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH, 944 Chestnut Ridge Road, Morgantown, West Virginia 26505.

Project Title:
Epidemiologic Study of Nonexposed Blue Collar Workers.

Principal Investigator:
Petersen, M.
Objective:
To (1) develop prediction equations for simple pulmonary function indices, proportion of subjects with various chest symptoms, and proportion of subjects with various x-ray abnormalities, based on race, sex, smoking status, age, height, weight, etc., for nonoffice personnel working in nearly clean environments; (2) develop similar equations for pulmonary function for the subset of asymptomatic nonsmokers; and (3) compare these to existing formulas in the literature.
Methods or Approach:
Plants willing to cooperate in the study will be selected from a list of plants in North Carolina that have reasonable numbers of employees working in low-exposure areas. This will require examination by an industrial hygienist. The data, consisting of chest x rays, simple spirometry, and a standard chest symptom questionnaire (MRC), will be collected by a mobile field team. After editing, the data will be analyzed using standard linear and logistic modeling techniques.
Results to Date:
Data have been collected. Prediction equations for symptom prevalence have been published, x-ray results have been submitted for publication, and the pulmonary function manuscript is going through final internal review.
Project Dates:
October 1976–1983.
Financial Support:
NIOSH (DI-541).
Reference:
Petersen, M.; Castellan, R.M. "Prevalence of Chest Symptoms in Nonexposed Blue-Collar Workers." *Journal of Occupational Medicine* 26(5):367-374, May 1984.

1544. DHHS, PHS, CDC, NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH, ALOSH, 944 Chestnut Ridge Road, Morgantown, West Virginia 26505.

Project Title:
Respiratory Effects of Exposure to Diesel Emissions in Underground Coal Miners.

Principal Investigator:
Ames, R.G.
Objective:
To determine acute and chronic respiratory effects from exposure to diesel engine emissions in underground coal miners.
Methods or Approach:
Since adequate control for cigarette smoking is required, several spinoff studies have been undertaken, including smoking cessation among coal miners as predicted by baseline respiratory function and symptoms (5-year prospective study) and effects of cigarette smoking cessation on 5-year pulmonary function changes in underground coal miners in the United States. Coal miners in Colorado, Utah, Wyoming, and Kentucky were studied in 1977 and again in 1982, providing a 5-year longitudinal design. Environmental samples of diesel engine contaminants were taken at both time periods. Respiratory health measures were determined by spirometry; respiratory symptoms were assessed through interviews. Five-year changes were assessed through logistic regression and least squares analysis.
Results to Date:
Presence of chronic respiratory symptoms at baseline was inversely related to cessation of smoking. Respiratory impairment was positively associated with smoking cessation, but failed to reach statistical significance. Some evidence of rebounding of forced expiratory volume in 1 sec was found following smoking cessation, but there was no effect on forced expiratory volume or on midexpiratory flow rate.
Future Plans:
The relationship between cigarette smoking, respiratory impairment, and lung cancer in coal miners will be studied.
Financial Support:
NIOSH.

1545. DHHS, PHS, CDC, NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH, ALOSH, Room 227, 944 Chestnut Ridge Road, Morgantown, West Virginia 26505.

Project Title:
National Study of Coal Miners' Pneumoconiosis.

Principal Investigator:
Attfield, M.
Objective:
To (1) study prevalence and longitudinal change in lung diseases among United States coal miners; (2) correlate levels and changes with possible factors such as indices of dust exposure and smoking; and (3) determine whether legal compliance levels are protective of the health of coal miners.
Methods or Approach:
The continuing epidemiological study of coal miners has gathered data in three surveys (1970-1981). In the fourth survey (1985), miners who were originally examined in the first two rounds will be traced and reexamined. This longitudinal cohort, which will include both current and ex-miners, will have been studied for a minimum of 15 years. Changes in measures of lung disease (spirometry, symptoms questionnaires, x rays) will be analyzed in relation to dust exposure and other factors. In addition, subsidiary analyses using DL_{co} and white noise will also be undertaken.
Results to Date:
Results from 9-year followup, which have been published, showed that (1) progression of pneumoconiosis is occurring at rates consistent with levels expected under current Federal dust compliance standard; and (2) patterns of lung disease are similar to those reported among miners in other countries (notably among British miners).
Project Dates:
October 1983–September 1988.
Financial Support:
NIOSH.

1546. VETERANS ADMINISTRATION, 1540 Spring Valley Drive, Huntington, West Virginia 25701.

Project Title:
Coal Workers Pneumoconiosis (CWP) - Pilot Study.

Principal Investigators:
Mufson, M.A.; Heydinger, D.K.
Objective:
To develop and test new quantitative and qualitative methods to characterize coal workers' pneumoconiosis.
Methods or Approach:
Long-time miners from West Virginia will be tested for pulmonary function using conventional measurements, radioactive tracer imaging, and ventilation and perfusion scanning. Initial evaluation by physical examination will be done in Huntington and the specialized pulmonary functions studies will be done at the Brookhaven National laboratory. Each miner will be tested for pulmonary function impairment by measuring lung volumes, FEV_1, MVV, V_{max}, V_{max25}, V_{max50}, RAW, MMF, gas exchange, and radioactive tracing imaging. The extent of pulmonary impairment will be evaluated in light of the number of years in the mines, whether the miner is a smoker or nonsmoker, and the type of coal seam mined. Pulmonary function tests that appear to correlate with these factors will be further evaluated among more miner volunteers.
Results to Date:
Of 35 retired coal miners tested, 25 were nonsmokers and 15 were smokers or ex-smokers; the nonsmokers had been exposed to coal dust for an average of 34 years. All miners had dyspnea on exertion; 8 had normal chest x ray, and 27 had some degree of abnormality of the lungs. Physical examination revealed only minor pulmonary abnormalities. Overall, the miners did not have any significant decrease in ventilatory function. Measurable functional impairment of the small airways was detected. Impaired gas exchange was the most significant functional abnormality; it was abnormal in all miners, including 18 at rest. All miners had increased alveolar-arterial oxygen gradients and were hyperventilating.
Financial Support:
VA.

Wisconsin

1547. MARQUETTE UNIVERSITY, COLLEGE OF NURSING, Milwaukee, Wisconsin 53233.

Project Title:
A Correlational Study of Group Cohesiveness and Smoking Cessation.

Principal Investigator:
Geiger, M.J.
Objective:
To investigate the relationship between group cohesiveness and cessation and reduction of smoking in smoking cessation workshop participants.
Methods or Approach:
The descriptive correlational study was conducted with 39 subjects selected through convenience sampling by participation in an American Lung Association of Wisconsin smoking cessation workshop at two midwestern institutions. Workshops consisted of six 2-hour sessions over a 4-week period. At the beginning of each session, participants privately reported to the leader self-monitored data regarding cessation success or failure (stating number of cigarettes smoked preceeding each workshop session). Information was also shared verbally within the group, followed by group applause for progress and effort. During the final session, participants completed a demographic sheet, the Group Environment Scale, and the Fundamental Interpersonal Relations Orientation-Behavior Scale.
Results to Date:
To test whether there was a correlation between individuals' perception of group cohesiveness and smoking cessation, a Point biserial correlation was performed and found to be significant at the 0.05 level ($r = 0.334$, $t = 2.09$), supporting the hypothesis of a significant positive correlation between an individual's perception of group cohesiveness and smoking cessation. Pearson product moment correlation revealed no significant correlation between group cohesiveness and smoking reduction ($r = 0.1617$, $p = 0.177$).
Project Dates:
July 1981–November 1984.
Financial Support:
St. Luke's Hospital, Milwaukee, Wisconsin.

1548. MARSHFIELD CLINIC, Department of Cardiology, Marshfield, Wisconsin 54449.

Project Title:
Smoking Cessation in Patients With Documented Coronary Heart Disease.

Principal Investigators:
Heath, G.W.; Moede, N.; Gangelhoff, T.
Objective:
To identify prevalence of smoking in a cardiovascular disease population; assess effectiveness of several approaches to smoking cessation in this group of patients.
Methods or Approach:
Methods being investigated include (1) behavior modification; (2) individual counseling with self-directed materials; and (3) hypnosis. Adjunctive use of nicotine gum is part of evaluation protocol. Descriptive followup of self-reported smoking behaviors for all approaches is being employed. Plans are being developed for a randomized approach to evaluation. Validation of smoking behavior will employ testing for carbon monoxide and serum thiocyanate.
Results to Date:
Project is in a preliminary phase.
Project Dates:
December 1984–December 1986.
Financial Support:
Marshfield Clinic.

1549. MEDICAL COLLEGE OF WISCONSIN, Division of Biostatistics Clinical Epidemiology, Milwaukee, Wisconsin 53226.

Project Title:
The Association of Smoking With Cardiomyopathy.

Principal Investigators:
Hartz, A.J.; Barboriak, J.J.; Anderson, A.J., et al.

Objective:
To investigate the possibility that smoking has an association with ventricular wall motion abnormalities that is independent of its known association with coronary occlusion.

Methods or Approach:
Subjects were 4,763 men between the ages of 35 and 74 who had diagnostic coronary angiography and ventriculography. Three kinds of wall motion abnormalities were considered: hypokinesis in one of four ventricular segments, hypokinesis in five to six ventribular segments (diffuse hypokinesis), and akinetic or dyskinetic wall motion in at least one segment.

Results to Date:
Among men younger than 55, the relative risk of diffuse hypokinesis was 2.78 (range 1.1 to 6.99) for heavy smokers compared with nonsmokers. Adjusting for the degree of coronary occlusion or eliminating subjects with a history of myocardial infarction did not change the relative risk. Among men who were 55 years or older, the relative risk (odds ratio for heavy smokers compared with nonsmokers) was not significant (0.55 to 2.28). Regardless of age, the relative risk of akinesis or dyskinesis, adjusted for coronary stenosis, was significant: 1.84 (range 1.28 to 2.65) for men under 55 and 1.57 (range 1.12 to 2.19) for men aged 55 or older. Results suggest that smoking is related to both cardiomyopathy and transmural myocardial infarction and that the relationships are largely separate from the association of smoking with coronary stenosis.

Project Dates:
March 1983–September 1984.

Financial Support:
Medical College of Wisconsin.

Reference:
Hartz, A.J.; Anderson, A.J.; Brooks, H.L., et al. "The Association of Smoking With Cardiomyopathy." *New England Journal of Medicine* 311(19):1201-1206, November 8, 1984.

1550. MOUNT SINAI MEDICAL CENTER, Room 414V, P.O. Box 342, Milwaukee, Wisconsin 53201.

Project Title:
Smoking Intervention Program for School Children.

Principal Investigators:
Leventhal, H.; Jackson, T.

Objective:
To reduce smoking-related morbidity and mortality by developing and fielding an effective school-based antismoking program.

Methods or Approach:
The program includes information on the immediate and long-term health effects of smoking, social skills training for resisting peer pressure to smoke, and the actual proportion of adolescents and adults who smoke. It also provides subjects with a knowledge base to enable them to interpret certain common smoking experiences as signs of bodily damage; attributes aversive reactions (coughing, etc.) to poisons in cigarettes; attributes symptom abatement (adaptation) to poisons that have destroyed the body's warning system. The goal is to train smokers to infer injury from symptoms or the absence of symptoms and to make the inference process automatic. The prevention program will be implemented in several urban middle schools and in one small town junior high school. Classrooms will be randomly assigned to either experimental or control condition. Subjects will be pretested, and posttests will be repeated at 6-month intervals throughout the study. Research design includes measures of process (how well or poorly messages are understood and accepted) and measures of outcome (smoking behavior and intention to smoke).

Results to Date:
Project is in a preliminary phase.

Project Dates:
June 1984–May 1987.

Financial Support:
NIDA (1R01DA03530).

1551. UNIVERSITY OF WISCONSIN, MADISON, WISCONSIN SURVEY RESEARCH LABORATORY, 610 Langdon Street, Madison, Wisconsin 53703.

Project Title:
Wisconsin Health Status Survey.

Principal Investigator:
Clarridge, B.

Objective:
To provide information on the health status of Wisconsin residents.

Methods or Approach:
A health risk factor assessment component of the survey containing questions on smoking, drinking, and eating habits was conducted by random digit dialing telephone interviews using computer-assisted techniques. Approximately 2,400 households were contacted; the first interview was with a randomly selected adult, who answered questions about him/herself, and then with the person most knowledgeable about the health of all members of the household, who answered questions about everyone in the household.

Results to Date:
The survey was completed in January 1985.

Financial Support:
Wisconsin Department of Health and Social Services.

1552. UNIVERSITY OF WISCONSIN, Department of Ophthalmology, 610 North Walnut Street, Madison, Wisconsin 53706.

Project Title:
Epidemiological Study of Diabetic Retinopathy.

Principal Investigator:
Klein, R.

Objective:
To study the epidemiology of diabetic retinopathy; evaluate data with respect to duration and age at diagnosis of diabetes, blood pressure level, and smoking history.

Methods or Approach:
A study of the prevalence and severity of diabetic retinopathy will be conducted in a group of 3,100 diabetic patients in their home communities. Objective recording of retinopathy by use of stereoscopic fundus photography combined with a standardized protocol for grading the retinopathy will be used. Grading of the stereo photographs will provide a sensitive and reproducible method for detection of retinopathy. The frequency and causes of visual impairment will be determined. The prevalence of retinopathy and of its various component lesions will be evaluated with respect to duration and age at diagnosis of diabetes, blood pressure level, and smoking history.

Results to Date:
The relationship between cigarette smoking and diabetic retinopathy has been examined in a preliminary analysis of the first 1,506 participants examined. Both Type I (age at diagnosis of diabetes < 30 years, $n = 467$) and Type II (age at diagnosis of diabetes ≥ 30 years, $n = 1{,}039$) participants were examined as part of a population-based study in southwestern Wisconsin.

Exposure data on cigarette smoking at the time of examination were derived from a set of questions about present or past smoking history, duration of smoking, and number of cigarettes smoked/day. Retinopathy status was determined according to the modified Airlie House classification. The rate of diabetic retinopathy varied from 21 percent (0-4.9 years duration) to 97 percent (≥ 15 years duration) in the Type I group and from 28 percent to 78 percent for comparable durations in the Type II group. There was no association between smoking history and duration of diabetes. In participants with Type I diabetes, the risk ratio estimate for the presence of retinopathy in smokers compared with those who had never smoked was 1.42 (95 percent C.L. 0.80-2.53); in participants with Type II diabetes it was 0.77 (95 percent C.L. 0.52-1.12). In participants with Type I diabetes the risk ratio estimate for the presence of retinopathy in ex-smokers compared to those who had never smoked was 1.74 (95 percent C.L. 0.80-3.89); in Type II participants it was 0.94 (95 percent C.L. 0.70-1.26). There was no relationship between the risk or severity of retinopathy and number of cigarettes smoked daily, or the number of pack-years smoked while diabetic. These data suggest that there is no excess risk of retinopathy in smokers or ex-smokers when contrasted with those who never smoked.

Future Plans:

The study population will be reexamined to describe incidence of retinal lesions, and vital status will also be followed.

Project Dates:

July 1979–1984.

Financial Support:

NEI (R01EY03083).

1553. UNIVERSITY OF WISCONSIN, MADISON, Department of Psychology, Madison, Wisconsin 53706.

Project Title:

Psychosocial Stressors, Smoking Cessation and CV Risk.

Principal Investigator:

Baker, T.B.

Objective:

To (1) determine whether prolonged central malaise is a necessary component of an aversive smoking procedure that produces optimal clinical outcome; (2) replicate previous research showing that posttreatment cardiac response to cigarettes is an accurate predictor of posttreatment abstinence; (3) determine whether the relationship between posttreatment abstinence and cardiac response to cigarettes depends on aversion therapy; and (4) determine effects of coping response training on short- and long-term clinical outcome.

Methods or Approach:

Chronic smokers (n=82) were randomly assigned to four groups: (1) full-scale rapid smoking and full counseling; (2) rapid puffing and full counseling; (3) truncated rapid smoking and full counseling; and (4) full-scale rapid smoking and reduced counseling (coping response training deleted). Outcome was assessed with posttreatment taste tests, psychophysiological measures, and followup telephone contacts with subjects and collaterals for 2 years posttreatment.

Results to Date:

Rapid smoking produced both intense malaise and prolonged habituation to cigarettes, while truncated rapid smoking produced only the former, and rapid puffing produced only the latter. Among subjects receiving full counseling, the best followup outcomes were achieved by rapid smoking, followed by rapid puffing and truncated rapid smoking. Results suggest that clinical effectiveness of aversive smoking is produced by both habituation and central malaise (taste aversion learning). Only subjects receiving full-scale rapid smoking showed enhanced cardiac response to cigarettes, and only for these subjects was cardiac response predictive of long-term outcome. Among subjects receiving full-scale rapid smoking, those receiving coping response training had better outcomes.

Future Plans:

Studies will compare the most effective rapid smoking intervention with nicotine gum administration and several different types of theoretically derived aversive smoking interventions. The impact of the coping response training program will be explored further.

Project Dates:

June 1982–continuing.

Financial Support:

NHLBI (1R01HL28519-01).

1554. UNIVERSITY OF WISCONSIN, MADISON, 750 University Avenue, Madison, Wisconsin 53706.

Project Title:

The Effects of Cigarette Smoke on Coronary Platelet Thrombosis.

Principal Investigator:

Folts, J.D.

Objective:

To (1) develop an animal model to simulate conditions that occur in patients with coronary artery disease; (2) demonstrate that narrowing of the coronary artery leads to platelet thrombi or clot formation, cutting off coronary flow leading to a heart attack; (3) ventilate anesthetized animals with cigarette smoke to show that smoke makes the clotting problem more severe; and (4) investigate drugs that might reduce clot formation.

Methods or Approach:

Several drugs that appear to inhibit clot formation will be studied; one may be found that will protect smokers from the increased clotting that normally occurs with smoking. Mechanisms that cause platelet clotting, in addition to cigarette smoke, are adrenalin or fats in the blood. If it can be determined how cigarette smoke activates clotting, it may lead to understanding other mechanisms involved. If it can be proved that smoking does something specific to provoke a heart attack, it may help some people to quit.

Results to Date:

Research evidence suggest that a special kind of clotting occurs in narrowed coronary arteries, leading to heart attack. An animal model has been established in which this special platelet clotting in partially obstructed coronary arteries can be produced. A way to blow cigarette smoke into animal lungs has also been developed, and it has been observed that the smoke makes clotting worse.

Future Plans:

Studies will be conducted to determine components in cigarette smoke that activate the clotting mechanisms and to compare effects of high tar and nicotine cigarettes with some of the new low tar and nicotine brands.

Project Dates:

July 1981–June 1982.

Financial Support:

AHA.

1555. UNIVERSITY OF WISCONSIN, MADISON, SCHOOL OF VETERINARY MEDICINE, 2015 Linden Drive West, Madison, Wisconsin 53706.

Project Title:
Lung Neuroendocrine Cell Innervation and Transplacental Response to Maternal Smoking.

Principal Investigator:
Keith, I.M.

Objective:
To evaluate innervation characteristics of lung neuroendocrine cells; test, in a hamster model, the hypothesis that in utero transplacental exposure to maternal smoking throughout pregnancy causes proliferation of pulmonary neuroendocrine cells that is significant at time of birth.

Methods or Approach:
Primigravid Syrian golden hamsters were placed in a Walton horizontal smoking machine four times/day from the 3rd to the 14th (penultimate) day of pregnancy. In three experiments, test groups inhaled mainstream smoke containing 0.37, 2.45, or 2.82 mg nicotine/cigarette. Control groups sham-smoked with an unlit cigarette. Neonates were sampled from all litters at age 0.5 to 5 hours, 3 days, and 6 days ($n=227$) and killed with sodium pentobarbitol. Serial paraffin sections of lungs were reacted with an argyrophil stain and with antiserotonin using an immunoperoxidase method. The numbers of single neuroendocrine cells (NEC) and groups of cells (NEB) that displayed argyrophilia (ARG) or serotonin-like immunoreactivity (SER) were determined relative to section surface area, and mean numbers of ARG cells and fractions of SER cells/NEB were recorded. Blood nicotine levels were determined in eight controls and six experimental animals of each treatment group.

Results to Date:
Neonates of mothers that smoked during pregnancy had significantly higher numbers of NEBs at 0.5 to 5 hours and 3 and 6 days postpartum. This increase was independent of neonate age and cigarette strength. The NEB increase was similar (17 percent) using either technique for visualization. Mean number of ARG cells/NEB was significantly elevated in neonates of smokers (11 percent) and was additionally increased by the strongest cigarette in 6-day-old animals (19 percent). This is of particular interest because, in contrast, numbers of ARG cells/NEB declined with age among controls. Also, the fraction of SER cells/NEB was significantly elevated (+9 percent) at all ages in those exposed to the strongest cigarette. Serum nicotine levels were dose dependent and similar to those measured in human heavy smokers.

Future Plans:
The hamster model will be used to determine if in utero transplacental exposure to maternal smoking throughout pregnancy predisposes to increased cancer risk later in life, and if such risk is enhanced if subjects become smokers. Specific emphasis will be placed on lung neuroendocrine tumors.

Project Dates:
January 1982–December 1984.

Financial Support:
CTR (1437).

1556. USDA, ARS, UNIVERSITY OF WISCONSIN, Madison, Wisconsin 53706.

Project Title:
Improving Safety of Cigar Tobacco by Genetic Principles and Cultural Practices.

Principal Investigators:
Newman, R.C.; Chaplin, J.F.

Objective:
To reduce or eliminate harmful exogenous chemical residues in tobacco leaves and smoke by cultural practices and by developing germplasm resistant to pest.

Methods or Approach:
Studies are conducted on Wisconsin cigar tobacco for pest control through breeding, cultural practices, and chemical means that leave little or no residues. New sucker control practices to eliminate or reduce residue are being developed. Treatments are evaluated for chemical and physical properties and residues. An acrylate polymer (Liqua-Gel) was dusted on tobacco seed moistened with peanut oil and seed was bulked with corn meal and sown. The polymer was mixed with water at the rate of 2 kg gel in 375 L of water. Tobacco transplants were pulled and washed free of soil, and the lower third dipped in gel prior to transplanting. Gel treated plants were transplanted with and without transplant water into moist field soil. Five soil incorporation methods were evaluated for tobacco field herbicide incorporation: cultimulcher, Chem Farm tread mulcher, spike tooth harrow, double disk-1 pass, and double disk-2 passes.

Results to Date:
All formulations and rates of maleic hydrazide for chemical sucker control resulted in 100 percent control; average sucker control for treatments that did not contain maleic hydrazide was 88.6 percent. Seedling emergence and plant stand was 10 percent more uniform than for untreated seed, and transplant size was reached 2 days earlier for treated seed. Treated plants were standing erect 24 and 36 hours after transplanting, but untreated plants were wilted. No differences in plant growth and development were found in the remainder of the growing season. Weed control was similar for all methods except use of the spike tooth harrow, which resulted in poorer grass and dicot weed control.

Project Dates:
August 1977–June 1984.

Financial Support:
USDA (7803-20881-006-A).

1557. VETERANS ADMINISTRATION MEDICAL CENTER, 2500 Overlook Terrace, Madison, Wisconsin 53705.

Project Title:
An Epidemiological Study of Diabetic Retinopathy.

Principal Investigators:
Chosy, J.J.; Klein, R.; Davis, M.D.

Objective:
To study the prevalence and severity of diabetic retinopathy and associated risk factors in a group of 2,400 diabetic patients in their home communities.

Methods or Approach:
In the first year of the study the number of diabetics living in an 11-county area was ascertained. In the second and third years of the study the population was studied. In the fourth and fifth year of the study the data were analyzed. In the sixth year of the study, beginning in July 1984, the cohort will be reexamined. Retinopathy will be recorded with stereoscopic fundus photographs combined with a standardized protocol for grading retinopathy. The association between the prevalence and severity of retinopathy and risk factors such as smoking and high blood pressure level will be examined, utilizing analysis of variance and other statistical techniques for multiple variables.

Results to Date:
The prevalence of retinopathy in insulin-taking persons diag-

nosed prior to 30 years of age varied from 17 percent in persons with diabetes for less than 5 years to 97.5 percent in those with diabetes for 15 or more years. The rate of proliferative retinopathy varied from 1.2 percent in persons with diabetes for less than 10 years to 56 percent in those with 30 or more years of the disease. Five percent of this population had high-risk characteristics for severe visual loss and 4 percent had the severest form of retinopathy resulting in the loss of vision in the eye. In those insulin-taking persons diagnosed prior to 30 yeas of age, the severity of retinopathy was associated with duration of diabetes, higher glycosylated hemoglobin, higher diastolic or systolic blood pressure level, the presence of proteinuria, and sex (male). No associations in this group were found between severity of retinopathy and cigarette smoking history, body mass index, amount or type of insulin, number of insulin doses per day, or number of past pregnancies.

Financial Support:
VA

1558. VETERANS ADMINISTRATION MEDICAL CENTER, 2500 Overlook Terrace, Madison, Wisconsin 53705.

Project Title:
Smoking Patterns and Beliefs Among Patients with Pulmonary Disease.

Principal Investigators:
Nerenz, D.R.; Hirschman, R.S.; Leventhal, H.

Objective:
To assess the frequency and nature of smoking among pulmonary disease patients, their motivation to quit, their beliefs about the relationship between smoking and their illness; determine the relationships among these beliefs, motivation, and smoking behavior.

Methods or Approach:
Sixty adult, English-speaking patients coming to the pulmonary clinic will be interviewed, one at a time, for 45 minutes. The interview includes questions on current smoking, smoking history, motivation to quit, and beliefs about the relationship between smoking and illness. Data will be entered by the interviewer onto a precoded form during the interview. Tape recordings of six interviews will be scored by a second coder to test for reliability. Data analysis will proceed in stages, including description of the sample, scale construction, and hypothesis testing.

Results to Date:
Data collection is just commencing.

Financial Support:
VA.

Wyoming

1559. UNIVERSITY OF WYOMING AT LARAMIE, Department of Psychology, Box 3415, University Station, Laramie, Wyoming 82701.

Project Title:
Discouraging Substance Use in Smokeless Tobacco-Prone Youth.

Principal Investigators:
Ksir, C.; McCarthy, W.J.; Gritz, E.R.

Objective:
To implement a primarily school-based intervention program in three schools in each of two communities in Wyoming to discourage teenagers from using tobacco products and alcohol.

Methods or Approach:
Three additional schools in each community will be used as controls. For males, focus will be on use of smokeless tobacco products, particularly canned moist snuffs. Interventions will be longitudinal, tailored to the different developmental needs of seventh, eighth, and ninth grade students, and will be implemented by teachers, coaches, and peer-nominated student counselors. Interventions are designed to increase students' perceived physical and social self-efficacy and to discourage adoption of a lifestyle associated with habits or physical addictions that limit subsequent choices. The program is planned for a 3-year period. In the first year, seventh grade students in experimental schools will receive traditional social inoculation training, and will be taught to be critical of prosmoking, protobacco use claims made by either peers or the media (especially billboard advertising) and to do individualized health monitoring. In the second year, eighth grade students will receive social skills training, communication skills training, and self-assertion training. In year 3, students will be taught decisionmaking skills and how to maintain an enduring positive self-image. Sex-specific anti-substance-use messages are included to capitalize on existing sex differences in smokeless tobacco use. Immediate posttest and annual follow-up questionnaires will collect data on lifestyle and health-related behaviors, memory for advertising, frequency of substance use, self-efficacy, self-image, need for achievement, need for affiliation, and need for autonomy. Information on brands of tobacco products used will also be collected.

Results to Date:
Pilot study data show greater smokeless tobacco use among seventh grade males than any other substance, including alcohol. Very few seventh grade females use smokeless tobacco products.

Future Plans:
Materials will be disseminated to other schools that wish to discourage substance use by students.

Project Dates:
December 1985–November 1990.

1560. UNIVERSITY OF WYOMING, Department of Psychology, Laramie, Wyoming 82071.

Project Title:
Chronic Nicotine Exposure: Behavioral and Biochemical Consequences.

Principal Investigator:
Ksir, C.J., Jr.

Objective:
To correlate elevations in brain nicotinic receptors with increased behavioral stimulation by nicotine.

Methods or Approach:
Rats are given daily injections of nicotine at varying doses for several days. Increases in stimulation produced are measured in photocell activity cages. Increased numbers of nicotinic cholinergic binding sites are measured using ^{3}H acetylcholine.

Results to Date:
Increases in both binding sites and behavioral stimulation are produced by doses of nicotine as low as 0.05 mg/kg/day for 5 days.
Project Dates:
December 1983–continuing.
Financial Support:
University of Wyoming.

1561. UNIVERSITY OF WYOMING, Department of Psychology, Laramie, Wyoming 82071.

Project Title:
Smokeless Tobacco Use in Adolescents.

Principal Investigator:
Ksir, C.J., Jr.
Objective:
To measure the incidence and correlates of smokeless tobacco use among junior high school students in Wyoming.
Methods or Approach:
Surveys were conducted in junior high schools.
Results to Date:
Among junior high school students in Cheyenne, 24 percent of males and 1 percent of females reported current use of smokeless tobacco compared with 7 percent of both males and females who reported being smokers.
Future Plans:
Intervention materials will be developed to prevent initiation of smokeless tobacco use.
Project Dates:
April 1982–continuing.
Financial Support:
University of Wyoming.

1562. UNIVERSITY OF WYOMING, Department of Psychology, Laramie, Wyoming 82071.

Project Title:
Psychopharmacology in a Model of Alzheimer's Disease.

Principal Investigator:
Ksir, C.J., Jr.
Objective:
To examine behavioral effects of nicotine sulfate and other behaviorally active drugs in rats with kainic acid lesions of the nucleus basalis magnocellularis.
Methods or Approach:
Rats are given kainic acid lesions in the nucleus basalis magnocellularis and tested for locomotor activity in photocell cages following injections of varied doses of nicotine or other drugs.
Results to Date:
Rats with nucleus basalis magnocellularis lesions are more stimulated by moderate doses of nicotine than control rats.
Future Plans:
Testing will be completed for dose–response effects of scopolamine, amphetamine, and morphine.
Project Dates:
January 1984–May 1985.
Financial Support:
NIMH (MH 39017).

ZAMBIA

1563. MUMBWA DISTRICT HOSPITAL, P.O. Box 830008, Mumbwa, Zambia.

Project Title:
Why People Should Stop Smoking - What Is Behind Smoking.

Principal Investigators:
Ndhlovu R.; Katenda, E.
Objective:
To (1) determine why some people smoke; (2) determine if people know effects of smoking; (3) investigate whether there could be a way to discourage smoking; and (4) discover whether smokers have ways of stopping smoking.
Methods or Approach:
A total of 38 males and 1 female in three work locations were interviewed; 9 were between 20 and 25 years of age, 9 between 25 and 30 years, and 21 were 30 years old or older. Questions were asked concerning influences on smoking initiation, consumption level, amount spent on cigarettes, cessation attempts, reasons for quitting, and success or failure of attempts to quit, knowledge of health effects, and suggestions for ways to reduce smoking.
Results to Date:
More than half smoked 5 to 10 cigarettes/day and 20 of the 39 had been smoking for more than 10 years. Friends who smoked and imitation of other smokers were the most influential factors in starting to smoke. High cost was the primary reason for wanting to quit (15 persons), but health concerns were also important. Of the 18 who responded to knowledge questions, 50 percent agreed that smoking played a role in heart disease, liver disease, diabetes, ulcers, prematurity, and lung cancer and that smoking could reduce life expectancy. The few suggestions for controlling smoking included vigorous antismoking campaign on mass media, stopping the manufacture of tobacco, and requesting assistance from the hospital.
Future Plans:
Antismoking advice will be provided at the workplaces visited. If successful, the project could be extended to other areas such as primary and secondary boarding schools.
Project Dates:
January 1985–February 1985.

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APPENDIX

Research resumes for the following projects were received too late to be completely processed for the 1984-1985 Directory of On-Going Research in Smoking and Health. However, the location of the sponsoring organization, the project title, and the principal investigators are provided so that direct requests for more information may be made if desired. The projects listed in the appendix are referenced in the Index of Principal Investigators only.

AUSTRALIA

1564. **EAST TORRENS DISTRICT CRICKET CLUB**, 195 North Terrace, Adelaide 5000, South Australia, Australia.

Project Title:
Campaign Against Tobacco Promotion Through Sport.

Principal Investigator:
Southwood, D.M.

1565. **FLINDERS MEDICAL CENTRE**, Department of Clinical Pharmacology, Bedford Park, Adelaide 5042, South Australia, Australia.

Project Title:
Methylxanthines and Cytochrome P-450 Isozymes in Man.

Principal Investigators:
Miners, J.O.; Birkett, D.J.

1566. **ROYAL NORTH SHORE HOSPITAL**, St. Leonards 2065, New South Wales, Australia.

Project Title:
Lung Inhomogeneity in Smokers.

Principal Investigator:
Berend, N.

1567. **MONASH UNIVERSITY**, Department of Psychology, Clayton, Victoria 3168, Australia.

Project Title:
Interactions Between Nicotine and Diazepam, Caffeine And Alcohol.

Principal Investigator:
White, J.M.

1568. **UNIVERSITY OF NEWCASTLE, FACULTY OF MEDICINE,** New South Wales 2308, Australia.

Project Title:
Randomized Clinical Trial of General Practitioner Interventions With Smokers.

Principal Investigators:
Sanson-Fisher, R.W.; Reid, A.L.A.; Redman, S.

1569. **UNIVERSITY OF NEWCASTLE, FACULTY OF MEDICINE,** New South Wales 2308, Australia.

Project Title:
Detection and Management of Smokers in General Practice.

Principal Investigators:
Sanson-Fisher, R.W.; Leeder, S.R.

1570. **UNIVERSITY OF NEWCASTLE, FACULTY OF MEDICINE,** New South Wales 2308, Australia.

Project Title:
A Randomized Clinical Trial of General Practitioner Interventions with Smokers Using Nicotine Chewing Gum.

Principal Investigators:
Redman, S.; Sanson-Fisher, R.W.

1571. **UNIVERSITY OF SYDNEY, PHARMACY DEPARTMENT,** Sydney, New South Wales 2006, Australia.

Project Title:
Studies on the Mode of Action of Carcinogenic Benzacridines and Dibenzacridines.

Principal Investigators:
Holder, G.M.; Ryan, A.J.

1572. **VICTORIAN SMOKING AND HEALTH PROJECT,** 1 Rathdowne Street, Carlton South, Victoria 3053, Australia.

Project Title:
Victorian Smoking and Health Project Guidelines and Directions and Goals for 1985.

Principal Investigator:
McAllister, K.

BRAZIL

1573. **MEDICAL ASSOCIATION OF BRAZIL,** Rua Sao Carlos do Pinhal 324, 01333 Sao Paulo, Brazil.

Project Title:
National Program Against Smoking.

Principal Investigators:
Mirra, A.P.; Rigatto, M.; Del Nero, E.

CANADA

1574. **HEALTH AND WELFARE CANADA, Health Promotion Directorate, Tobacco Unit, Room 444, Jeanne Mance Building, Tunney's Pature, Ottawa, Ontario K1A 1B4, Canada.**

Project Title:
Peer Assisted Smoking Prevention Project.

Principal Investigator:
Health and Welfare Canada.

1575. **HEALTH AND WELFARE CANADA,** Health Promotion Directorate, Tobacco Unit, Room 444, Jeanne Mance Building, Tunney's Pasture, Ottawa, Ontario K1A 1B4, Canada.

Project Title:
Generation of Non-Smokers Guide Book of Project Ideas for Community Groups.

Principal Investigators:
Canadian Cancer Society; Health and Welfare Canada.

1576. **HEALTH AND WELFARE CANADA,** Health and Welfare Directorate, Tobacco Unit, Room 444, Jeanne Mance Building, Tunney's Pasture, Ottawa, Ontario, K1A 1B4, Canada.

Project Title:
Preschool Smoking Prevention Project.

Principal Investigators:
Health and Welfare Canada; Canadian Cancer Society.

DENMARK

1577. **AARHUS UNIVERSITY,** Institute of Medical Microbiology, DK-8000 Aarhus C, Denmark.

Project Title:
Serum Antibodies to Aspergillus Fumigalus in Danish Farmers.

Principal Investigators:
Schonheyder, H.; Moller-Hansen, C.; Andersen, P., et al.

1578. **AARHUS UNIVERSITY,** Institute of Medical Microbiology, DK-8000 Aarhus, Denmark.

Project Title:
Serum Antibodies to Pigeon Antigens in Smokers and Nonsmokers.

Principal Investigators:
Andersen, P.; Christensen, K.M.

1579. **FINSEN INSTITUTE,** Department of Dermatology, Strandboulevarden 49, DK-2100 Copenhagen 0, Denmark.

Project Title:
Cessation of Smoking Enhances Sister Chromatid Exchanges in Lymphocytes.

Principal Investigators:
Wulf, H.C.; Husum, B.; Niebuhr, E.

1580. **FINSEO INSTITUTE,** Strandboulevarden 49, DK-2100 Copenhagen 0, Denmark.

Project Title:
Sister Chromatid Exchanges in Smokers of High-Tar Cigarettes, Low-Tar Cigarettes, Cheroots and Pipe Tobacco.

Principal Investigators:
Wulf, H.C.; Husum, B.; Niebuhr, E.

INDIA

1581. **CANCER RESEARCH INSTITUTE,** Tata Memorial Centre, Parel, Bombay 400 012, India.

Project Title:
Modifying Effects of Diet on Upper Alimentary Tract Cancer in Persons Who Chew and Smoke Tobacco.

Principal Investigators:
Notani, P.N.; Jayant, K.

1582. **GUJRAT AGRICULTURAL UNIVERSITY,** Tobacco Project and Department of Biochemistry, Anand 38810, Gujrat State, India.

Project Title:
Lipid Changes in a Growing Tobacco Plant.

Principal Investigators:
Chakraborty, M.K.; Tewar, M.

1583. **GUJRAT AGRICULTURAL UNIVERSITY,** Tobacco Project and Department of Biochemistry, Anand 38810, Gujrat State, India.

Project Title:
Effect of Cultural Practices and Product Modifications on Bidi Smoke Chemistry.

Principal Investigators:
Chakraborty, M.K.; Ghelani L.M.

1584. **GUJRAT AGRICULTURAL UNIVERSITY,** Tobacco Project and Department of Biochemistry, Anand 38810, Gujrat State, India.

Project Title:
Enzymic Modification of Bidi Tobacco.

Principal Investigators:
Chakraborty, M.K.; Ghelani, L.M.

ITALY

1585. **CENTRO STUDIO E PREVENZIONE ONCOLOGICA,** Viale A. Volca 171, 50131
Firenze, Italy.

Project Title:
Smoking Habits in Occupational Categories in Tuscany.

Principal Investigators:
Chellini, E.; Costantini, A.; Mazzoni, G., et al.

1586. **ITALIAN LEAGUE AGAINST CANCER,** Florence, Viale A. Volta 171, 50131
Firenze, Italy.

Project Title:
Health Promotion Research for the Prvention and Control of Adolescent Cigarette Smoking.

Principal Investigators:
Zanzari, P.; Chellini, E.; Buiatti, E.

1587. **POLICLINICO S. ORSOLA,** Clinica Medica III, Department of
Gastroenterology, Via Massarenti 9, 40138 Bologna, Italy.

Project Title:
Modifications of Salviary Gland Secretion Induced by Tobacco Smoking.

Principal Investigators:
Callegari, C.; Lami, F.

1588. **POLICLIMICO S. ORSOLA,** Clinica Medica III, Department of
Gastroenterology, Via Massarenti 9, 40138 Bologna, Italy.

Project Title:
Effect of Cigarette Smoking on Exocrine Pancreatic Function.

Principal Investigators:
Callegari, C.; Lami, F.

1589. **UNIVERSITY OF ROME,** Department of Pediatrics, Allergy and Clinical Division, Viale Regina Elena 329, Rome 00161, Italy.

Project Title:
Parental Smoking and Atopic Disease in "At Risk" Newborns for Atopy.

Principal Investigators:
Businco, L.; Bruno, G.; Benincori, N., et al.

JAPAN

1590. **KURUME UNIVERSITY, SCHOOL OF MEDICINE,** Department of Public Health, 67 Asahi-machi, Kurume City 830, Fukuoka, Japan.

Project Title:
The Role of Drinking and Cigarette Smoking in the Excess Deaths From Liver Cancer.

Principal Investigators:
Shibata, A.; Hirohata, T.

NEW ZEALAND

1591. **CHRISTCHURCH CLINICAL SCHOOL OF MEDICINE,** Christchurch Public Hospital, Christchurch, New Zealand.

Project Title:
The Christchurch Child Development Study.

Principal Investigator:
Fergusson, D.M.

1592. **OTAGO UNIVERSITY,** Dunedin Multidisciplinary Health and Development Research Unit, Dunedin, Otago, New Zealand.

Project Title:
Longitudinal Study of Initiation, Maintenance and Voluntary Extinction of Smoking Behaviour on Nine-Year-Old Children in Dunedin.

Principal Investigators:
Tian, P.S.; Silva, P.

NORWAY

1593. **UNIVERSITY OF BERGEN, RESEARCH CENTER FOR OCCUPATIONAL HEALTH AND SAFETY**, Hans Tanksgt. 11, 5000 Bergen, Norway.

Project Title:
The Relationship Between Work Injuries/Illnessess and Harmful Effects of Smoking.

Principal Investigator:
Berg, G.

POLAND

1594. **MEDICAL ACADEMY IN BYDGOSZOZ**, Department of Allergology and Internal Diseases, Bydgoszcz, ul. Ujejskiego 75, Poland.

Project Title:
The Immunologic Response to Tobacco Antigens in Smokers.

Principal Investigators:
Romanski, B.; Zbikowska, M.; Sinkiewicz, W.

1595. **M. SKLODOWSKA-CURIE INSTITUTE OF ONCOLOGY**, Oncology Centre, Wawelska 15, Warsaw, Poland 00-973.

Project Title:
Smoking Frequency and Patterns in Poland, 1985.

Principal Investigator:
Zatonski, W.

1596. **M. SKLODOWSKA-CURIE INSTITUTE OF ONCOLOGY**, Oncology Centre, Wawelska 15, Warsaw, Poland 00-9/3.

Project Title:
Smoking Frequency and Related Attitudes Among Medical Doctors in Poland.

Principal Investigators:
Zatonski, W.

1597. **M. SKLODOWSKA-CURIE ISTITUTE OF ONCOLOGY,** Oncology Centre, Wawelska 15, Warsaw, Poland 00-973.

Project Title:
Tar, Nicotine and Carbon Monoxide in Polish Cigarettes, 1983-85.

Principal Investigators:
Zatonski, W.; Leppanen, A.

1598. **M. SKLODOWSKA-CURIE INSTITUTE OF ONCOLOGY,** Oncology Centre, Wawelska 15, Warsaw, Poland 00-973.

Project Title:
Passive Smoking and the Level of Cotinine in Urine Samples in Non-Smoking Women.

Principal Investigator:
Zatonski, W.

SWEDEN

1599. **UNIVERSITY HOSPITAL,** Research Laboratory, Department of Obstetrics and Gynecology, S-221 85 Lund, Sweden.

Project Title:
Specific Placental Plasminogen Activator Inhibitor.

Principal Investigators:
Astedt, B.; Lecander, I.

1600. **UNIVERSITY OF LUND,** Malmo General Hospital, Department of Surgery, Medicine, and Clinical Pharmacology, Malmo, Sweden.

Project Title:
Influence of Cigarette Smoking on Goiter Formation, Thyroglobulin, and Thyroid Hormone Levels in Women.

Principal Investigators:
Christensen, S.B.; Ericsson, U.-B.; Janzon, L.; et al.

UNITED KINGDOM

1601. **CITY OF SHEFFIELD MDC EDUCATION DEPARTMENT**, Leopold Street, P.O. Box 67, Sheffield, England.

Project Title:
Evaluation of the Health Education Council "My Body Project" (Final Phase).

Principal Investigators:
Wilcox, B.; Gillies, P.A.

1602. **ROYAL FREE HOSPITAL, SCHOOL OF MEDICINE**, Department of Clinical Epidemiology and General Practice, London NW3 2PF, England.

Project Title:
British Regional Heart Study.

Principal Investigators:
Shaper, A.G.; Pocock, S.J.; Code, D.G., et al.

1603. **UNIVERSITY OF MANCHESTER**, Department of Nursing, Stopford Building, Oxford Road, Manchester MI3 9PT, England.

Project Title:
Giving Up Smoking: An Exploration of Support Systems for Nurses.

Principal Investigators:
Faulkner, A.; Booth, K.

UNITED STATES

1604. **LOMA LINDA UNIVERSITY**, Loma Linda, California 92350.

Project Title:
Symptoms of Chronic Obstructive Pulmonary Disease Associated With Exposure to Secondhand Cigarette Smoke.

Principal Investigators:
Magie, A.R.; Abbey, D.E.; Euler, G.L., et al.

1605. **OHIO DEPARTMENT OF HEALTH,** Division of Chronic Diseases, P.O. Box 118, Columbus, Ohio 43216.

Project Title:
Survey of Smoking Policies in Ohio High Schools.

Principal Investigator:
Capwell, E.M.

1606. **OHIO DEPARTMENT OF HEALTH,** Division of Chronic Diseases, P.O. Box 118, Columbus, Ohio 43216.

Project Title:
Survey of Smoking Policies in State Health Department, Ohio Local Health Departments, and Ohio Health Organizations.

Principal Investigator:
Capwell, E.M.

1607. **ST. RITA'S MEDICAL CENTER,** 730 West Market, Lima, Ohio 45801.

Project Title:
Smoke Free.

Principal Investigator:
Elstro, C.

1608. **UNIVERSITY OF WASHINGTON,** Department of Psychiatry and Behavioral Sciences, Seattle, Washington 98195.

Project Title:
Perinatal Psychoactive Drug Use: Effects on Gender, Development, and Function in Offspring.

Principal Investigator:
Martin, J.C.

1609. **UNIVERSITY OF WASHINGTON,** Department of Psychiatry and Behavioral Sciences and Biostatistics, Seattle, Washington 98195.

Project Title:
Saccharin Preferences in Food Deprived Aging Rats are Altered as a Function of Perinatal Drug Exposure.

Principal Investigators:
Martin, J.C.; Martin, D.C.; Sigman, G., et al.

1610. **UNIVERSITY OF WASHINGTON,** Department of Psychiatry and Behavioral Sciences and Biostatistics, Seattle, Washington 98195.

Project Title:
Interactive Effects of Chronic Maternal Ethanol and Nicotine Exposure Upon Offspring Development and Function.

Principal Investigators:
Martin, J.C.; Martin, J.C.; Charo, S., et al.

1611. **UNIVERSITY OF WASHINGTON,** Department of Psychiatry and Behavioral Sciences and Biostatistics, Seattle, Washington 98195.

Project Title:
Voluntary Activity in the Aging Rat as a Function of Maternal Drug Exposure.

Principal Investigators:
Martin, J.C.; Martin, D.C.

INDEX OF PRINCIPAL INVESTIGATORS

Aagaard, J., 0164
Aaro, L.E., 0416
Abbey, D.E., 1604
Abboud, R.T., 0107, 0110-0115
Abelin, T., 0492, 0493
Abood, L.G., 1284, 1286
Abraham, E., 0260
Abrams, D.B., 1431, 1432
Abramson, J.H., 0312
Aceto, M.D., 1511
Acevedo, A., 0139-0141
Adams, D.R., 0868
Adams, J.D., 1200
Adams, J.E., 0796
Ades, A., 0529
Adhvaryu, S.G., 0272
Adiga, K.R., 0842
Adriaanse, H., 0401
Afroza, M.S., 0051
Agha, B.J., 0902
Aghi, M.B., 0291
Agne-Traub, C.E., 1512
Agnew, J.E., 0550, 0551
Ahlund, C., 0456
Aigner, K., 0049
Ainslie, G.W., 1427
Akers, R., 0873
Akiyama, E., 0362
Albanes, D., 0986
Albert, R.E., 1260
Alcayaga, M.P., 0141
Alexandrov, A.A., 0502
Allegra, L., 0323
Allen, C.L., 0078
Allen, W.A., 1395
Altman, R., 1172
Ames, R.G., 1544
Amler, R., 0810
Ampry, F.R., 0782
Amsel, Z., 1387
Anderhalt, R., 1343
Andersen, C., 0169
Andersen, P., 1577, 1578
Andersen, R., 0898
Andersen, R.A., 0881
Anderson, A.J., 1549
Anderson, H.R., 0555
Anderson, J.M., 0584
Anderson, P.J., 0624
Andersson, K., 0454
Ando, K., 0356, 0357
Andre, E., 0478
Andrews, J.L., Jr., 1071, 1072
Andrews, R.L., 1219, 1524
Aneshensel, C.S., 0686
Angst, J., 0494
Anthoisen, N.R., 1006
Aoki, K., 0350, 0351
Arabi, M.A., 0448
Arai, T., 0364, 0376
Araiso, T., 0364
Araki, S., 0381, 0382
Aranda, C.P., 1297
Aravanis, C., 0252
Archer, V.E., 1492
Arciti, C., 0334-0336
Arena, J.G., 0807
Armstrong, B.G., 0529
Arnesen, E., 0420
Arnold, C.B., 1100, 1243
Aronow, W.S., 1152
Asal, N.R., 1363
Asano, M., 0368-0372
Ashley, M.J., 0138
Asmussen, I., 0159, 0170-0172
Astedt, B., 1599
Ataharuddin Ahmed, Q., 0051
Atkinson, W.O., 0926
Attfield, M., 1545
Auerbach, O., 1177-1180
Auth, J.B., 0796
Autrup, H., 0157, 0158
Awotedu, A.A., 0406
Axell, T., 0476
Axelson, O., 0453, 0470
Aycock, M.K., Jr., 1028
Azama, F., 0636, 0637

Bachman, J.G., 1104
Badellino, F., 0324
Baer, J.S., 1376, 1380
Baer, L., 1075
Baer, L.S., 1224
Bahna, S.L., 0958, 0963
Bailey, A., 0534
Bailey, G.J., 1535
Bailey, W.C., 0614
Bailey, W.J., 0859, 0860
Baines, C.J., 0123
Baird, W.M., 0862
Baker, A.L., 0848
Baker, H.L., Jr., 1115
Baker, T.B., 1553
Balar, D.B., 0269
Balestra, D.J., 1506
Balfour, D.J.K., 0584, 0587
Balko, A., 1439, 1440
Banasik, R., 0432
Banks, R.O., 1358
Banoczy, J., 0262
Baragiola, A.M., 0002
Barboriak, J.J., 1549
Bardell, D., 1168, 1169
Barefoot, J.C., 1308
Barker, L.R., 0994
Barnes, M.V., 0072, 0073
Barnett, C., 0652
Baron, J., 0871, 0872
Barrett-Connor, E., 0698, 0701
Barrett, P., 0566
Bars, M.P., 1170
Bartelik, M., 0436
Bartelik, S., 0436, 0437
Bartlett, E.E., 0607
Bartsch, H., 0337
Baskin, A., 0747
Batten, L., 0576
Battig, K., 0481, 0482, 0484-0487
Bauchinger, M., 0177
Baudier, F., 0229
Bauman, K.E., 1323
Bausell, R.B., 1396
Beach, T.F., 1348, 1355
Beaty, H.N., 1497
Becker, A.H., 1106
Becker, J.F., 1102
Becker, M.H., 1496
Becker, S., et.al., 0874
Beckerman, R., 0965
Beehler, C.J., 0759
Beems, R.B., 0396
Beg, M.H.A., 0424
Begin, R., 0103
Begleiter, A., 0314
Behera, D., 0276, 0278, 0281
Beilin, L., 0047
Belch, J.J.F., 0586
Belcher, D.W., 1535, 1536
Belcher, M., 0557
Bell, P., 1030
Ben-Tal, T., 0304
Benditt, E.P., 1522, 1526
Benedek, I.H., 0899
Benet, L.Z., 0672
Bengtsson, C., 0464
Benhamou, E., 0228
Benhamou, S., 0228
Benincori, N., 1589
Bennett, C.H., 0904
Bennett, G., 0807
Bennett, M.H., 0540
Bennett, S.A., 0016
Benowitz, N., 0672
Benowitz, N.L., 1017
Benwell, M.E.M., 0584
Berend, N., 1566
Berenson, G.S., 0959
Berg, G., 1593
Berger, E.M., 0759
Berglund, G., 0473, 0474
Bergstrom, J., 0455
Berman, S.M., 0808

References following all entries are to Description Numbers.

INDEX OF PRINCIPAL INVESTIGATORS

Bernstein, D.A., 0852
Berrino, F., 0320, 0326, 0327
Berry, G., 0565
Bertera, R.L., 0786
Best, J.A., 0089, 0127, 0129
Bhide, S.V., 0266
Bhu, N., 0284
Bianchi, C., 0318, 0348
Bird, C.C., 0510
Birkett, D.J., 1565
Bishop, D.B., 1150
Bisson, G., 0103
Biswas, D.K., 1064
Bittesini, L., 0318, 0348
Bittoun, R., 0026, 0027
Bjelke, E., 0417
Bjorntorp, P., 0463
Blache, D., 0230
Black, A., 0074
Black, O., Jr., 0827
Blackburn, H.W., 1120
Blair, A., 1011
Blake, R.L., Jr., 1143
Blake, S., 1122
Blankenhorn, D.H., 0719
Blitzer, P.H., 1067
Bloom, J.W., 0619
Blot, W.J., 0142, 0988, 0989
Blouin, P., 0899
Blount, W.R., 0798
Blow, C.M., 0537
Bobo, J.K., 1527
Bock, F.G., 0603
Boer, H.R., 1312
Boffetta, P., 0346
Bohachick, P.A., 1426
Booth, D.C., 0887
Booth, K., 1603
Borgman, R.F., 1444
Borkan, G.A., 1046
Bos, R.P., 0402
Bosisio, E., 0328
Bosse, R., 1046, 1065
Bossi, R., 0323
Bottaro, P., 0335
Botvin, G.J., 1233-1235
Bourke, G.J., 0296
Boyd, A., 0585
Boyd, E.J.S., 0580
Boyd, G.M., 0744
Boyko, E.J., 1537
Bracken, M.B., 0772, 0774
Brady, J.V., 0996
Braga, P., 0323
Bragonier, R.J., 0692
Brain, J.D., 1076
Brand, R.J., 0676
Brandange, S., 0477
Brandspiegel, D., 1384
Brastins, E., 1424
Braughler, J.M., 1352
Breitenstein, B.D., 1530
Breslow, L., 0690
Bresnick, E., 1154-1158
Breviario, F., 0322
Bridges, R.B., 0905-0908
Brischetto, C.S., 1369
Brollo, A., 0318, 0348
Bronson, D.L., 1502
Brook, D., 1222
Brook, D.W., 1245, 1246
Brook, J.S., 1222, 1245, 1246, 1248
Brooke, O.G., 0555
Brooks, P.E., 0516
Bross, K.J., 0180
Brown, C., 0973
Brown, C.H., 0995
Brown, E.R., 0688
Brown, H.L., 0012-0015
Brown, K.S., 0127
Brown, L.M., 0988
Brown, T.E., 0078
Brownell, K.D., 1411
Brownfield, C.A., 0788
Bruce, R.M., 1151
Bruhn, J.G., 1477, 1482
Brunnemann, K., 0250
Brunnemann, K.D., 1197, 1211
Bruno, G., 1589
Brunswick, A.F., 1225
Bryant, D., 0027
Bryant, L.R., 1446
Bryant, M.S., 1077
Buchner, A., 0314
Buehler, J.W., 0809
Buffler, P.A., 1472-1474, 1478
Buiatti, E., 1586
Buist, A.S., 1370
Buist, S., 1127
Bull, H.A., 0536, 0537
Bulpitt, C.J., 0056
Bulzebruck, H., 0186, 0187
Bunn, J.M., 0928
Burch, J.D., 0091, 0093
Burch, P.R.J., 0564
Burchfiel, C.M., 1105
Burgess, W.A., 1061
Burghard, G., 0232, 0233, 0235
Burke, T.A., 0716
Burr, W.A., 1095
Burrows, B., 0617
Burton, D., 1193, 1194
Burton, H.E., 0949
Burton, H.R., 0925, 0929, 0950
Bush, L.P., 0922, 0943
Bush, P.J., 0779, 0780
Bush, T.L. 1000
Businco, L., 1589
Buta, J.G., 1292
Butler, P., 1480
Butterworth, C.E., Jr., 0606
Buzzi, R., 0483
Byartveit, K., 0411
Byers, T., 1275, 1276
Byrd, L.D., 0817
Cady, L.D., 0718
Cagliani, F., 0335
Cain, W.S., 0766
Calderon-Solt, L., 0841
Callegari, C., 1587, 1588
Calman, A., 0589
Calnan, M., 0518
Calvert, J., 0926
Camic, P.M., 1089
Campbell, E.J., 1140
Campbell, I.A., 0593, 0594, 0600
Campbell, P., 1338
Campbell, S.C., 0621
Cannon, D.J., 0630, 0631
Capwell, E.M., 1605, 1606
Caraballoso, M., 0985
Carel, R., 0315
Carey, K.D., 1467
Carleton, R.A., 1430
Carlson, H.F., 0746
Carmichael, S., 0589
Carmody, T., 1369
Carr, L.A., 0941
Carter, H.W., 1179
Carter, W.B., 1536
Cartier, A., 0084
Cartwright, R.A., 0510
Carver, T., 1312
Casada, J.H., 0952
Casperson, C., 0813
Castagnoli, N., Jr., 0708
Castelli, W.P., 0987
Castleden, W.M., 0020
Castonguay, A., 1199, 1208
Castro, J.A., 0001
Catanelli, M., 0342
Cavelier, C., 0244
Cerutti, P.A., 0488
Chakraborty, M.K., 0268
Chamberlain, M.J., 0136
Chamberlain, W.J., 0822
Chameaud, J., 0242
Chan, T.V., 0082
Chan, W.C., 0259
Chance, B., 1409, 1412
Chansin, R., 0497
Chaplin, J.F., 0943, 0946, 0951, 0953, 1331,
  1556
Charlton, A., 0531, 0532
Charo, S., 1610
Chaturvedi, A.K., 1340
Chauncey, H.H., 1097
Cheek, P.R., 1368
Chellini, E., 1585, 1586
Chen, F.-M., 1449
Chen, H.Z., 0146, 0147
Chen, M.-F., 0088
Cheng, A.L.S., 1034
Chernick, V., 0117
Cheung, N.K., 1185
Chiang, M.L., 0665
Chijimatsu, Y., 0377
Child, J., 0681

INDEX OF PRINCIPAL INVESTIGATORS

Chilvers, C., 0518
Chlap, Z., 0428
Choi-Lao, A.T.H., 0122
Cholewka-Cabaj, K., 0433
Chomicka, Z., 0427
Chopra, N.M., 1317
Chortyk, O.T., 0806, 0821, 0822, 0924
Chosy, J.J., 1557
Chowdhury, P., 0627, 0628
Christensen, J.L., 0157
Christensen, K.M., 1578
Christensen, S.B., 1600
Christie, D., 0035
Chu, F., 0761
Chun, N., 0864
Chung, F.-L., 1201
Chung, S.I., 1280
Church, D.F., 0961
Chyle, M., 0151
Chyle, P., 0151
Clark, K., 0006
Clark, V., 0689
Clarke, E.A., 0124
Clarke, J.C., 0027
Clarke, P.B.S., 0983
Clarke, S.W., 0550, 0551
Clarridge, B., 1551
Clausen, J.A., 0670
Clayton, B.E., 0577
Cleary, P., 1074
Clelland, R.C., 1410
Cluette-Brown, J.E., 1082
Coates, T.J., 0712
Cockcroft, D.W., 0105
Code, D.G., 1602
Coggins, C.R.E., 0479, 0480
Cohen, B.H., 0997, 0998, 1005, 1007, 1151
Cohen, B.S., 1261
Cohen, D., 1076
Cohen, P., 1248
Cohen, S., 1378, 1385
Cohen, S.J., 0861
Cohn, S.H., 1298
Colditz, G.A., 1079
Cole, P., 0546
Cole, P.V., 0552
Colella, S., 0322
Colley, J.R.T., 0560
Collins, A.C., 0757
Collins, G.B., 0901, 0911
Collins, J.F., 1475
Collins, R., 0547
Collishaw, N.E., 0067, 0074, 0080
Colombi, A., 0340
Comstock, G.W., 1000, 1001, 1314
Connett, J., 1123
Connolly, C.K., 0511, 0512
Connor, J., 0776
Conrad, E.E., Jr., 1366
Constantinescu, V., 0444
Cooreman, J., 0226, 0232, 0233-0236, 0240
Copeland, R.M., 0041
Cornuau, P., 0238
Correa, P., 0960, 1478
Correy, J., 0045
Corrigna, K., 0855
Corson, J., 0102
Costa, M., 1483
Costabel, U., 0180
Costantini, A., 1585
Cotton, D.J., 0105
Coulson, A., 0689
Counsilman, J.J., 0041
Cowan, R., 1266
Cowing, D.E., 0970
Coyle, M., 1332
Cracknell, N.G., 0506, 0544
Cribb, A., 0532
Criqui, M.H., 0699, 0700
Crombie, I.K., 0582
Crosignani, P., 0320
Crotti, N., 0325
Crow, C.S., 0611
Crowdy, J.P., 0539
Csinos, A.S., 0824
Cullen, K.J., 0008
Cummings, K.M., 1267, 1268
Cummings, S.R., 0712
Cunningham, L., 1243
Curnen, M.G.M., 0770
Curphey, T.J., 1163
Curran, J., 0045
Curran, J.P., 1436, 1441
Curry, S.G., 1529

D'Esopo, N., 0768
D'Hondt, W., 0055
D'Onofrio, C., 0675
Dalaker, K., 0418, 0419
Daling, J.R., 1518
Dalton, J., 1326
Daly, L., 0298-0301, 0303
Daly, M., 0295
Danaher, B., 0646
Daniel, S.S., 1231
Darrall, K.G., 0527
Dave, S., 0470
Davidson, F.R., 0779
Davies, F., 0595
Davis, A.W., 0940
Davis, D.L., 0920, 0923, 0924, 0933, 0945, 0948
Davis, G.S., 1497, 1499
Davis, J.W., 1146
Davis, K., 1523
Davis, L.D., 0932
Davis, M.D., 1557
Davis, S., 1520
Dawley, H.H., Jr., 0967, 0968
Day, C.L., Jr., 1073
Day, R.W., 1516
De Backer, G., 0057, 0058, 0059
De Flora, S., 0337-0339
De Guire, L., 0086
De Jong, D.W., 1033
De Maio, A., 0249
De Mouzon, J., 0227
De Vries, H., 0398
De Witte, L., 0401
Deans, G., 0589
Deaton, J.E., 1508
Debusk, R.F., 0654
Decarli, A., 0331, 0332
Decker, B., 0880
DeCosimo, D., 1086
Dejana, E., 0321, 0322
Delormas, P., 0478
DeLucia, A.J., 1446
DeMaria, A.N., 0887, 0888
Dembo, R., 0798
Deng, J., 0143
DeShazo, R.D., 0964
Deslypere, J.P., 0054
Detels, R., 0682
Detre, K.M., 1416, 1423
Devereax, T.R., 1315
Dewey, J.E., 0863
DeWit, H., 1089
Dhand, R., 0279
Di Sant'Agnese, P.A., 1288
Diamond, E.H., 1151
Diamond, L., 0900
Diaz Gomez, M.I., 0001
Dickson, R.C., 0901
Dielman, T.E., 1103
DiFranza, J.R., 1092
Digenis, G.A., 0902
Dische, S., 0540
Disler, P.B., 0447
Ditzel, J., 0156
Dlin, R., 0313, 0316
Doerken, H., 0185
Doherty, S.J., 0842
Domino, E.F., 1107
Donati, M.B., 0321
Donfield, S., 1382, 1383
Donnelly, G., 1085, 1089
Donnelly, G.M., 1429
Donovan, R.J., 0015
Dorough, H.W., 0889
Dosman, J.A., 0105
Doukas, M., 0886
Doyle, E., 0039
Doyle, M.P., 1470
Dragsted, L., 0158
Drake, E.R., 0073
Drawbaugh, R.B., 1471
Driscoll, S.G., 1051
Drop, M.J., 0401
Du Mazaubrun, C., 0237
Dulac, J., 1506
Dulfano, M.J., 1296
Dumont, E., 0229, 0230
Dunn, A.G., 0018, 0019
Dunn, B.P., 0066
Dunn, J.D., 0957
Dunn, P.A., 0018, 0019

INDEX OF PRINCIPAL INVESTIGATORS

Durrer, D., 0399
Dutton, R.E., 0094, 0095
Dwyer, T., 0009
Dyer, N., 0507

East, J.R., 0524-0526
Ebert, R.V., 0622, 0629, 0633
Eckel, R.H., 0762
Edling, C., 0453, 0470
Edwards, G.L., 1495
Effeney, D.J., 0738
Eggleston, J.C., 1026
Ehrengruber, H., 0492
Eide, G.E., 0417
Einisto, P., 0194
Eiser, J.R., 0562, 0563
Ekstrom-Jodal, B., 0471
Ekwo, E.E., 0870
El-Bayoumy, K., 1202
El-Gendawy, H.S.A., 0581, 0588
Elashoff, J.D., 0650
Elferink, J.G.R., 0400
Elkind, A.K., 0558, 0559
Elliot, J.M., 0062
Ellis, K.J., 1221
Ellis, N., 0578
Elmfeldt, D., 0473, 0474
Elst[illegible], C., 1607
Elwood, J. M., 0070
Elwood, P.C., 0598
Emmett-Oglesby, M.W., 1468
Emmons, K.M., 0852, 0866
Emurian, H.H., 0996
Enarson, D., 0116
Eneroth, P., 0454
Ensminger, M.E., 0995, 1002
Enstrom, J.E., 0666, 0684, 0685
Epstein, L., 0305-0307
Eraker, S.A., 1496
Ercan, Z.S., 0500
Ericsson, U.-B., 1600
Ernhart, C.B., 1344
Ershoff, D, 0646
Ershow, A., 0988
Ertel, N.H., 1186
Erwin, V.G., 0763
Eschwege, E., 0239
Etscorn, F.T., 1188
Etzel, R.A., 1324
Euler, G.L., 1604
Evans, R., 0880
Evans, W.H., 0527
Everson, R.B., 1313
Ewart, C., 0994
Eysenck, H.J., 0566, 0567
Eysenck, S.B.G., 0566

Fagerstrom, K.-O., 0468
Fahy, B.F., 0615
Fairshter, R.D., 0679
Falkler, W.A., Jr., 1029
Fann, W.E., 1488
Fanning, C.J., 0788
Farrell, G.C., 0042
Faulkner, A., 1603
Fechter, L.D., 1003
Fee, W.M., 0583
Feldman, B.M., 1124
Feldman, M.J., 1294
Feldman, R S., 1097
Fell, R.D., 0934, 0942
Fera, T., 0110, 0111, 0113, 0115
Ferencz, C., 1025
Fergusson, D.M., 1591
Ferm, V.H., 1164
Ferrence, R.G., 0061
Ferris, B.G., Jr., 1061, 1063
Fertman, C.I., 1421
Feshbach, S., 0696
Field, G.B., 0017
Field, W E., 0519
Fielding, J.E., 0691
Figa-Talamanca, I., 0330
Filipy, R.E., 1515
Fine, B.J., 1081
Fine, L., 0846
Fine, R., 1475
Finkelstein, M.M., 0096
Fischman, M.W., 0847
Fischman, S.L., 1282
Fisher, D., 0015
Fisher, E.B., Jr., 1150
Fisher, S.E., 1262
Fitzgerald, G.A., 1458
Flamant, R., 0228
Flay, B.R., 0724-0729
Fletcher, R.D., 1424
Flick, D., 0803
Flora, J.A., 0664
Flores, A., 0070
Floss, H.G., 1353
Flynn, B.S., 1501-1504
Foa, V., 0340
Folgero, S., 0409
Follick, M.J., 1431
Folts, J.D., 1554
Forbes, C.D., 0586
Forbes, W.F., 0128
Ford, J., 0691
Forde, O.H., 0420
Forsberg, S., 0206
Forss, M., 0192
Fortmann, S.P., 0660, 0662
Fouillet, X., 0480
Fouts, J.R., 1315, 1316
Fowler, G., 0548, 0570-0572
Fox, H., 1228, 1238
Fox, N.L., 1023
Fox, W.N., 0508
Frank, A.L., 1462
Frank, R., 0062
Frankel, J.W., 0609, 0800
Frankowski, R.F., 1478
Franks, A.L., 0812
Franzblau, C., 1044
Frasca, J.M., 1179, 1180
Fraser, C.O., 0079
Fraser, H.S., 0053
Fraumeni, J.F., Jr., 0989
Frazier, D.T., 0892, 0893
Frecker, R., 0496
Freedman, B.D., 1218
Freeman, G., 0653
Freigang, W.F., 0179
Freitas, J.P., 0439, 0440
Fried, P.A., 0071-0073
Friedman, G.D., 0641
Frischman, S.L., 1274
Frost, F., 1539
Fryers, P., 0063
Frymoyer, J.W., 1500
Fuchsberg, R.R., 0979, 0980
Fujimoto, I., 0355
Fujimoto, W.Y., 1528
Fujino, T., 0990
Fukui, J., 0376
Furbush, W., 0970
Furst, A., 0717
Fuxe, K., 0454

Gaines, T.P., 0823
Gairola, C., 0903
Gaiser, J., 0403
Gal, P., 1312
Gala, C.L., 1287
Galante, E., 0319
Galdston, M., 1259, 1297
Gallavan, R.H., Jr., 1357
Gallus, G., 0319
Gandevia, B., 0017
Gangelhoff, T., 1548
Gao, Y.-T., 0142, 0143
Gardner, G.C., 1462
Gardner, G.J., 0005
Gardner, J.W., 1019
Garfinkel, L., 1177, 1178, 1195
Garland, C., 0701
Garner, D.W., 0843
Garro, A., 1293
Garvey, A.J., 1065, 1066, 1094
Gazit, D., 1282
Geiger, M.J., 1547
Gelbart, S., 0857
Gellert, G., 0351
Gennser, G., 0469
Gentry, E., 0816
Geokas, M.C., 0734
Gergely, I., 0261
Geslin, P., 0219
Geyer, J., 1363
Ghebrehiwet, B., 1281
Ghelani, L.M., 1583, 1584
Gibberd, R.W., 0039
Gilbert, G.G., 1374

INDEX OF PRINCIPAL INVESTIGATORS

Gilbert, J.R., 0089, 0129
Gilchrist, L.D., 1527, 1532, 1533
Gilhotra, R.S., 0280
Gillies, P.A., 0568, 0569
Gillies, P.M., 0588
Gillis, C.R., 0590, 0591
Ginsberg, D., 0707
Giovino, G., 1268
Giuntini, C., 0337
Glantz, S.A., 0709, 0710
Glaros, A.G., 0794, 0795
Glasgow, R.E., 1339, 1371
Glazer, E.R., 0665
Glueck, C.J., 1356
Goldberg, R., 1084, 1092
Goldberg, R.J., 1091
Goldberg, R.L., 1087
Goldberg, S.R., 1013, 1014
Goldbourt, U., 0308
Goldenberg, R.L., 0610
Goldman, B., 1236
Goldsmith, J.R., 0304
Goldstick, T.K., 0839
Gonzalez-Rothi, R.J., 0802, 0803
Goodger, B.M., 0516
Goodman, G.E., 1517
Goodman, M.T., 1216
Gordon, I., 0035
Gordon, J.R., 1529
Gori, G.B., 1016, 1017
Gorlick, B., 1166
Gorsky, M., 0314, 0714, 0715
Gottlieb, A., 0663
Goutet, M., 0224
Graham, I., 0297, 0303
Graham, K., 0134
Graham, S., 1273-1276
Grant, M.M., 1249
Gray, N.J., 0003, 0004
Greaves, I.A., 1061
Greenberg, R.A., 1324
Greenberg, S.D., 1461
Greenblatt, D.J., 1080
Greenspan, D., 0702, 0715
Greenspan, J., 1263, 1264
Greer, R.O., Jr., 0756
Gregor, F., 0069
Grgurinovich, N., 0030
Griffin, P.J.A., 0595
Griffith, E.E., 0787
Griffith, R.B., 0894
Griffiths, R.R., 0992
Grimaldi, B., 0219
Grimaud, C., 0220
Grise, V.N., 0784
Gritz, E.R., 0666-0669, 0690, 1559
Grossman, L.M., 0726
Grossman, M.L., 1182
Grove, J.H., 0946
Grube, J.W., 0294
Gruder, C.L., 0850
Grufferman, S., 1306, 1310
Grunberg, N.E., 1020
Grunfeld, B., 0418, 0419
Guengerich, F.P., 1453
Guerin, M.R., 1447
Guidotti, T.L., 0106
Guirgis, H.A., 0678
Gulati, S.M., 0274
Gullvag, B.M., 0421, 0422
Gulovali, M.G., 0499
Gunasegaram, R., 0392
Gunduz, G., 0499
Gunn, R.C., 1108-1110
Guo, G., 0146
Gupta, P.C., 0286, 0287, 0289, 0290
Guth, P.H., 0748
Gvozdjak, J., 0155
Gvozdjakova, A., 0155
Gwynn, G.R., 1321, 1331

Hackney, J.D., 0649
Haddow, J.E., 0969
Haertzen, C.A., 0991
Hafer, R.F., 1539, 1540
Hagerup, L., 0168
Hagino, N., 1479
Haines, A.P., 0546
Haines, C.S., 0994
Hajek, P., 0557
Hale, K.A., 1138
Haley, N.J., 1203, 1209, 1215
Hall, C.B., 1287
Hall, R.G., 0739, 0741
Hall, S.M., 0703, 0707
Hall, W.J., 1287
Hallett, R., 0504
Hallstrom, T., 0464
Halper, A., 1135
Hamilton, J.L., 0881, 0891, 0921, 0922, 0943, 0951
Hammons, R.O., 0805
Hanai, A., 0355
Hann, N.E., 1362
Hanne, N., 0316
Hansen, J.E., 0640
Hansen, W.B., 0724, 0725, 0727, 0728
Hao, X., 0145
Haoy, S., 0407
Harada, T., 0367
Hardinge, M.G., 0645
Hargreave, T.B., 0592
Harley, N.H., 1261
Harmes, K., 0506, 0544
Harrington, G.W., 1404
Harris, C.C., 0982
Harris, C.M., 1468
Harris, J.O., 0801-0803
Harris, M., 0025
Harrison, K.L., 0048
Hart, R.R., 0749
Hartge, P., 1009, 1010
Hartman, C.R., 1146
Hartz, A.J., 1549
Hassan, M., 1058
Hassanein, K.M., 0878
Hataway, C.J., 0605
Hatchell, P.C., 0818
Hatsukami, D.K., 1118, 1125
Haughey, B., 1273
Hauknes, A., 0407
Haussmann, R., 0188
Hauth, J., 1471
Hauth, J.C., 1471
Hawach, F., 1059
Hawthorne, V.M., 0590, 0591
Hay, D.L., 0940
Hay, D.R., 0404
Hayashi, M., 0386
Hayashi, Y., 0358
Haynes, A., 0991
Haynes, S., 0814
Health and Welfare Canada, 0083
Heath, G.W., 1548
Hebel, J.R., 1022
Hecht, S.S., 1204-1206, 1253
Heckman, C.A., 1343
Hedin, C.A., 0461, 0476
Hedley, A.J., 0581
Hedrick, B., 0747
Heicke, 0185
Heim, C.R., 1452
Heimburger, D.C., 0606
Heiner, D.C., 0958, 0963
Heinhold, J.W., 1066, 1094
Heinonen, O.P., 0986
Heinrichs, W.L., 0658
Heller, J., 0553
Hellman, R., 1272, 1283
Helsing, K.J., 1314
Henderson, B.E., 0721, 0730-0732
Henderson, F.W., 1324
Henderson, P.T., 0402
Hendrix, W.H., 1442
Hennekens, C.H., 1053, 1054
Henningfield, J.E., 1012
Hennon, D., 1382
Hensleigh, P.A., 0652, 0657
Henson, P.M., 0753
Henson, T.H., 1445
Henson, W.H., 0882, 0925, 0952
Herbert, F.A., 0075
Herity, B., 0296
Herivan, R., 0444
Herman, S.M., 0435
Hersey, P., 0028
Herskovic, J.E., 0693, 0694, 0736
Hertz, M.I., 1119
Heydinger, D.K., 1546
Hickey, J., 0991
Hickey, N., 0297-0301, 0303
Hickey, R.J., 1410
Hickman, R., 1465
Higashi, E., 0375
Higenbottam, T.W., 0544
Higgins, C.W., 0957
Higgins, I.T.T., 1105

INDEX OF PRINCIPAL INVESTIGATORS

Higgins, M.W., 1105
Hill, D.J., 0004, 0005, 0011
Hill, J.S., 0135
Hiller, F.C., 0624
Hilt, B., 0413
Hinds, M.W., 0830, 0832, 0833
Hirohata, T., 1590
Hirokawa, A., 0372
Hirsch, G.L., 0640
Hirschman,R.S., 1558
Hirvonen, L., 0206-0210
Hjermann, I., 0414
Ho, J.H.C., 0257, 0258
Hobbins, J.C., 0772
Hobel, C.J., 0692
Hodgson, J.T., 0515
Hoey, J.R., 0090
Hoffman, D., 1184
Hoffmann, D., 0250, 1196-1198, 1200, 1202, 1203, 1206-1211
Hogelin, G., 0816
Hogg, J.C., 0101, 0108
Hogstedt, C., 0460
Hogue, C.J.R., 0808, 0809
Hoidal, J.R., 1119, 1450
Hojnacki, J.L., 1082
Holder, G.M., 1571
Hole, D.J., 0590, 0591
Hollenberg, P.F., 0838
Hollis, J., 1367
Hollo, I., 0261
Hollowell, J.G., 0876
Holly, E.A., 0711
Holm, I., 0414
Holmes, F.F., 0879
Holmes, G.E., 0877-0879
Holmstrup, P., 0163
Holroyd, J., 0680
Holt, C., 1380
Homma, H., 0377, 0378
Honck, P., 1465
Honma, Y., 0366
Hoover, R., 0989, 1009, 1010
Hopkins, R.H., 1542
Hops, H., 1372
Hornby, A.P., 0066
Horsfield, K., 0509
Horton, R., 0668
Horvath, W.J., 1103
Hoss, W.P., 1285
Hotchkiss, J.H., 1291
Houston-Miller, N., 0654
Howe, G.R., 0091, 0093, 0123
Howe, H.H., 1255
Hrubec, Z., 0459, 1011
Hsu, S.C., 1405
Hua, L.S., 0144, 0145
Huber, E., 0189
Huchon, G.J., 0651
Hughes, J.R., 1126, 1136
Hughes, S.L., 1165
Hugod, C., 0184
Humble, J.W., 0905
Hunkeler, E., 0643
Hunt, L.A., 0937
Hunter, S.M., 0959
Hurley, J., 1509
Hurych, J., 0154
Husgafvel-Pursiainen, K., 0194, 0195
Husum, B., 1579, 1580
Hutchison, A.A., 0793
Hutchison, G.B., 1067
Huttunen, J.K., 0204, 0986
Hyde, G.L., 0955

Iannotti, R.J., 0779
Iizuka, H., 0357
Ikeda, M., 0388, 0390
Inatomi, K., 0378
Innes, K.S., 0072
Inui, T.S., 1536
Ioffe, S.V., 0117
Ip, M.P.C., 1247
Irvine, S., 1396
Ishizu, Y., 0373
Israel, R.H., 1271
Ivankovic, S., 0175
Iwamoto, E.T., 0909

Jacka, E., 0447
Jackson, S., 0070
Jackson, T., 1550
Jacobs, J.E., 0840
Jacobson, B., 0505
Jacobson, E.D., 1357, 1358
Jain, M., 0092
James, L.S., 1228, 1231
Jamrozik, K., 0571, 0572
Janerich, D.T., 1295
Janoff, A., 1280, 1281
Jansen, A., 0418, 0419
Janzon, L., 1600
Jardim, J.R.B., 0060
Jarvik, M.E., 0681, 0683, 0693, 0694, 0696, 0736, 0737, 0746
Jarvis, M.J., 0522
Jasinski, D.R., 1012
Jayant, K., 1581
Jedrychowski, W., 0433, 0434
Jenkins, B., 0599
Jenkins, R.A., 1447
Jenner, P.G., 0520
Jenouri, G., 0791
Jensen, L., 0710
Jensen, R.G., 1290
Jephcott, R.W., 0007
Jepsen, A., 0158
Jindal, S.K., 0275-0277
Johal, S.S., 0112-0114
Johnson, C.A., 0724, 0725, 0727-0729
Johnson, R., 1081
Johnston-Earl, R.N., 0785
Johnston, L.D., 1104
Joly, O.G., 0985
Jones, G., 0948
Jones, J.R., 0863
Jones, R.A., 0897
Jones, R.D., 0515
Jones, R.M., 0513
Jones, R.T., 0703-0706
Jongen, W.M.F., 0394
Jongeneelen, F.J., 0402
Jonstone, D.A., 0580
Joris, I., 1090
Juchau, M.R., 1522

Kabat, G.C., 1216
Kafalas, T., 1218
Kafatos, A.G., 0251
Kahn, K., 1083
Kalandidi, A., 0254-0256
Kamat, S.R., 0292, 0293
Kameswara Rao, B.V., 0267, 0268
Kaminski, M., 0237, 0238
Kandel, D., 1232
Kaneko, M., 0385
Kannas, L., 0416
Kannel, W.B., 0987
Kanner, R.E., 1127
Kantor, A., 1009
Kaprio, J., 0203
Kapur, K.K., 1097
Kararck, T.W., 1377
Kari-Koskinen, O., 0208
Kariniemi, V., 0192, 0202
Karl, P., 1262
Kashyap, S., 0277
Kasperbauer, M.J., 0883, 0898, 0929
Katenda, E., 1563
Kato, S., 0356
Kaufert, J., 0118
Kauffman, F.C., 1027
Kaufman, D., 1039
Kaufman, S., 1274
Kawaguchi, T., 0360
Kawakami, Y., 0365
Kawamoto, J., 0359
Kay, C.R., 0549
Kayser, K., 0186, 0187
Kazantzis, G., 0529
Keeler, R.F., 1494
Keil, U., 0176
Keintz, M.K., 1386
Keith, I.M., 1555
Keith, R.E., 0604
Kellam, S.G., 0995
Kelleher, R.T., 1055
Kelly, N.L., 1079
Kelsey, S., 1423
Kelson, S.R., 1341
Kent, S., 0599
Kerr, D., 1383
Kerr, H.D., 1024
Kessler, I.I., 1026

INDEX OF PRINCIPAL INVESTIGATORS

Kettunen, R., 0210
Kew, R., 1281
Key, C.R., 1189
Keyser, D.J., 1149
Khadim, M.I., 0425
Khandelwal, P.D., 0284, 0285
Khandelwal, S., 0284, 0285
Khoury, M.J., 1005, 1007
Kiehne, E.C., 0786
Kilburn, K.H., 0722, 0723
Killen, J.D., 0659, 0662, 0663
Kim, H.C., 0415
Kim, K.H., 0442
Kimizuka, G., 0358
Kind, P.R.N., 0556
King, A.C., 0664
King, J.M., 1466
Kinnman, J., 0462
Kira, S., 0376, 0378
Kirkbride, J., 0068
Kischer, K., 1368
Kitamura, S., 0377
Kjaeldgaard, A., 0451
Kjelsberg, M.O., 1123, 1128-1130
Klaiber, E.L., 1098
Klausen, K., 0169
Kleevens, J.W.L., 0259
Klein, R., 1552, 1557
Kleinerman, J., 1247
Kleinman, J.C., 0976
Kleisbauer, J.P., 0241, 0248
Klepp, K.-I., 1122, 1135
Klesges, R.C., 1339, 1371
Kline, J., 1257
Kling, H., 0453
Klintenberg, C., 0457
Klisiewicz-Panszczyk, T., 0426
Klugman, P.J., 1167
Kneip, I.J., 1258
Knight, G.J., 0969
Knill-Jones, R.P., 0581, 0588
Knobf, M.K.T., 0773
Knopper, M., 0645
Knott, V.J., 0098
Knox, D.L., 1004
Knudson, R.J., 0619
Kobrick, J.L., 1081
Kodama, M., 0385
Koepsell, T.D., 1537
Koh, H.K., 1073
Kok, G.J., 0398
Koley, J., 0264, 0265
Kolonel, L.N. 0830-0833
Kono, S., 0388, 0390
Koo, L.C., 0258
Kopetzky, M.T., 1469
Korelitz, B.I., 1239
Kornitzer, M., 0057-0059
Koskela, K., 0198
Koskenvuo, M., 0203
Koski, O.R., 1459
Kotake, A.N., 0848
Kottke, T.E., 1137
Kovatch, R.M., 0993
Koyama, T., 0364
Kozak, J.T., 0153
Krause, F., 0179
Kristein, M.M., 1278, 1279
Krohn, M.D., 0873, 0874
Krokje, A., 0422
Krumdieck, C.L., 0606
Krzyzanowski, M., 0434
Ksir, C.J., Jr., 1559-1562
Kuc, J., 0930
Kucharska, J., 0155
Kuhnert, B.R., 1345
Kuhnert, P.M., 1345
Kulle, T.J., 1024
Kuller, L.H., 1418, 1425
Kumar, R., 0521
Kumpfer, K., 1493
Kundsin, R.B., 1051
Kune, G.A., 0032-0034, 0036
Kune, S., 0032-0034, 0036
Kung, S., 1032
Kunze, M., 0050
Kunze, M.J., 0050
Kupusalo, E., 0205
Kurata, J.H., 0650
Kuroishi, T., 0352
Kusama, M., 0374
Kusiak, R., 0097
Kuwata, K., 0361, 0362
Kyaeldgaard, A., 0450

L'Abbe, K.A., 0090
La Vecchia, C., 0331, 0332
Laaser, U., 0312
Lachenbruch, P.A., 0870
Lagomarsino, L., 0325
Lagrue, G., 0219
Lajtha, A., 1250-1252
Lal, H., 1468
Lal, N., 0273
Lam, J.J., Jr., 1328
Lam, T., 0259
Lambert, N.M., 0673
Lami, F., 1587, 1588
Landau, L.I., 0023
Lando, H.A., 0866, 0867
Lang, F., 0490
Langard, S., 0413
Lange, A., 0429, 0430
Langinvainio, H., 0203
Lapidus, L., 0464
Lappi, T., 0205
Largay, B.P., 1015
Larson, P.J., 0644
Larsson, A., 0461
Larsson, B., 0450, 0451, 0472
Lasater, T.M., 1430
Laskey, W.K., 1408
Lasser, N., 1171
Lauer, R.M., 0873, 0874
Lauzon, R.R.J., 0069
LaVoie, E.J., 1198, 1200, 1210
Lavstedt, S., 0456
Lawrance, L., 0851
Layden, T.J., 0856
Lazaro, C., 1242
Le Houezec, J., 0249
Leaf, A., 1074
Lebovits, A.H., 1223
Lebowitz, M. D., 0617, 0618
Lecander, I., 1599
Lee, C.J., 0885
Lee, H.K., 0068
Lee, J.H., 0830
Lee, L.-Y., 0893, 0917
Lee, P.N., 0519
Lee, T.-H., 0442
Lee, Y.H., 0441
Leeder, S.R., 0040, 0044, 1569
Lefcoe, N.M., 0130, 0131, 0137, 0138
Leggett, E., 0921
Leggett, J.E., 0898, 0950, 0953
Lehr, R.E., 1365
Lehrer, S., 0966
Lehtovirta, P., 0192, 0193
Leichtman, A.P., 1342
Leinweber, C., 0063
Lellouch, J., 0225
Lelong, N., 0237, 0238
Lemen, R., 0620
Leppanen, A., 1597
Lerner, J.V., 1393, 1394
Leung, F.W., 0748
Levallois, M., 0240
Leventhal, H., 1550, 1558
Levine, B.E., 0615
Levine, E.A., 1147
Levy, D.A., 0997
Levy, E., 0304
Levy, J.C., 1171
Levy, L., 0687
Lewis, B., 0761
Lewis, C.E., 0697
Lewis, L., 1495
Lewit, E.M., 1176
Lewthwaite, C.J., 0539
Li, W.X., 0147
Liang, J., 1113
Liard, R., 0234
Lichtenstein, E., 1372, 1376-1380
Lickrish, G.M., 0124
Lie, K.I., 0399
Lieber, C.S., 1293
Liener, I.E., 1117
Lijinsky, W., 0993
Lilis, R., 1244
Lin, P.P., 0927
Lindquist, B.E., 1359
Lindsay, G.B., 1495
Linn, W.S., 0649
Linnainmaa, K., 0196
Lippmann, M., 1260
Lisiewicz, J., 0431, 0438

INDEX OF PRINCIPAL INVESTIGATORS

Litt, I., 0658
Little, R.E., 1525
Littlefield, J., 1217
Litton, P.D., 0883
Livingston, G.K., 1489
Livson, N., 0670, 0674
Lloyd, B., 0577, 0578
Lloyd, F.S., 0577, 0578
Lochsen, P.W., 0408-0410
Lock, P.M., 1523
Loda, F.A., 1327
Loeppky, R.N., 1144, 1145
Logston, D.N., 1242
Lombrail, P., 0239
Long, G.Y., 0144, 0145
Longanath, A., 0392
Longenecker, G.L., 0612, 0613
Lopez-Majano, V., 0094
Lorup, J.R., 0163
Lourenco, R.V., 0853, 0854
Low, R.B., 1498
Lowe, J.B., 0607
Lowe, N., 0743
Lowe, R.H., 0881, 0949
Lowrey, A.H., 0783
Loysen, E., 0528
Lozada, F., 0714
Lubaway, W.C., 0890
Lubin, J.H., 0985
Luepker, R.V., 1133
Lukas, R.J., 0616
Lukas, S.E., 1056
Lundgren, J., 0457
Lunell, N.-O., 0449
Luzzatto, L., 0317
Lyager, S., 0166
Lynch, C.J., 1016, 1017
Lynn, D.G., 1309
Lynn, W.R., 0972, 0974
Lynn, W.S., 1309
Lyon, J.L., 1019, 1490, 1491
Lyons, E., 0600

Mabuchi, K., 1026
Maccoby, N., 0659, 1062
Machin, S.J., 0538
Mackay, E.V., 0041
MacKown, C.T., 0944, 0945
Maclure, K.M., 1060
MacMahon, B., 0254, 0256, 1060
Madison, R., 0635
Madsen, H., 0156
Magie, A.R., 1604
Magnani, C., 0317
Mahoraj, D., 0053
Maier, R.H., 1311
Maisiak, R.C., 0605
Maita, K., 0367
Majno, G., 1090
Malhotra, M.S., 0292
Malik, S.K., 0275-0281
Malo, J.-L., 0084
Maltzman, I., 0744
Manchester, D.K., 0758
Mandelstam, P., 0954
Manetti, M., 0328
Manfreda, J., 0081
Mangelsdorff, A.D., 1466
Mannisto, J., 0214
Mansouri, A., 0623
Marcus, A.C., 0666, 0667, 0690
Marlatt, G.A., 1529
Marlowe, C., 0936
Maron, M.B., 1352
Maroni, M., 0333, 0340
Marshall, J., 1273, 1275, 1276
Marshall, M.V., 1467
Marshall, W.R., 1325
Marstein, S., 0423
Martell, E.A., 0752
Martin, A.R., 0712
Martin, D.C., 1609, 1610, 1611
Martin, H., 0785
Martin, J.C., 1608, 1609, 1610, 1611
Martin, J.E., 1139
Martin, J.L., 1408
Martin, T.R., 1538
Martin, W.R., 0910
Marty, M.A., 0763
Marty, P., 0625
Maruo, T., 0379
Marzillier, J., 0548, 0570
Mashberg, A., 0345, 1181-1184
Masironi, R., 0496
Maslow, W.C., 0636, 0637
Mason, T., 1350
Massey, T.E., 1315, 1316
Masuko, K., 0379
Matsubara, J., 0384
Matsukura, S., 0380
Matsuo, T., 0373
Matsushita, H., 0387
Matter, S., 0934, 0942
Matthew, K., 1418
Matthys, H., 0180
Mattison, D.R., 0626
Matulionis, D.H., 0895, 0896
Maulik, D., 1288
Mausner, B., 1384
Mauss, A.L., 1542
May, J.T., 1362
Mayberry, J., 0599
Maymon, T., 0310
Mazzoni, G., 1585
McAlister, A. L., 1062, 1481
McAllister, K., 1572
McCann, B., 0102
McCarthy, W.J., 0634, 0669, 0688, 0691, 0695, 0696, 1559
McClure, W.F., 1318
McCoy, G.D., 1347
McCubbin, H., 1134
McDaniel, H.G., 0608
McDermott, R.J., 0844
McDonagh, P.F., 1469
McDowell, I., 0074, 0121
McEwen, J., 0523
McGarry, J., 0545
McGrath, D., 1307
McGrath, J.J., 1469
McIntyre, K.O., 1379
McKee, C., 1035
McKenna, T.A., 0068
McKeown Eyssen, G.E., 0124
McLeod, K.W., 1443
McNabb, M.E., 0622, 0629, 0632, 0633
McNamara, P., 0899
McNeill, J., 0749
McNelly, E.A., 0771
McSharry, C., 0585
Mead, P.B., 1504
Meade, T.W., 0541
Meares, R.A., 0031
Meberg, A., 0423
Medici, T.C., 0489
Meehan, T., 1102
Meenihan, R.J., 1383
Mehrotra, S.K., 0263
Mehta, F.S., 0286-0291
Meigs, R.A., 1346
Meilahn, E.N., 1425
Melamed, M.R., 1241
Melander, A., 0458
Melikian, A.A., 1212
Melinte, L., 0444
Mellies, M.J., 1356
Mello, N.K., 1056
Mendelson, J.H., 1056
Mendoza, F., 0658
Menkes, H.A., 0998
Merletti, F., 0345-0347
Merletti, F.D., 1183
Mermelstein, R.J., 1378, 1379
Merrill, W.W., 0768, 0769
Mettlin, C., 1269
Meudt, W.J., 1292
Meyer, C.D., 1426
Meyer, J.S., 1484-1487
Michel, C., 0482, 0484
Michnich, M., 1530
Midanik, L., 0643
Milgrom-Friedman, J., 0031
Miller, A.B., 0091-0093, 0123
Miller, G.H., 1397-1403
Miller, H.C., 0877, 0878
Miller, R.K., 1288
Mina, G., 0334
Mincer, H.H., 1459
Minelli, L., 0341
Miners, J.O., 1565
Mir, M.A., 0601, 0602
Mirra, A.P., 1573
Mirvish, S., 1160
Miskella, J., 0579
Mitchell, A.A., 1043, 1052
Mitchell, H., 1423
Mitchell, J.A., 1111

INDEX OF PRINCIPAL INVESTIGATORS

Mittler, J.C., 1186
Mittman, C., 0635
Mochizuki, M., 0379
Modeer, T., 0456
Modolo, M.A., 0330, 0341, 0342
Moede, N., 1548
Mogielnicki, R.P., 1505, 1506
Mohla, S., 0781, 0782
Mohr, P., 1161
Molimard, R., 0249
Moller, K., 0160
Moller-Hansen, C., 1577
Mommsen, S., 0164
Monarca, S., 0342, 0343
Monarca, S., 0343
Monson, R.R., 1051
Monteith, D., 1338
Montes, M., 1295
Monti, P.M., 1432
Moore, C., 0938
Moore, L.G., 0755
Morasso, G., 0324, 0325
Moreton, W.J., 0525, 0526
Morgan, M., 0294
Morgan, M.V., 1189
Moriarity, M., 0296
Morra. M.E., 0773
Morrill, J.H., 0775
Morris, J., 1448
Morris, J.F., 1381
Morrison, B.J., 0076
Morrison, J.A., 1356
Morrison, S.A., 0836
Morrow, R., 1270
Morse, D.E., 1021
Morse, W.H., 1055
Morton, W.E., 1375
Moses, L., 0652
Moskowitz, J.M., 0647, 0648
Mothersgill, C., 0121
Moulin, J.-J., 0243, 0244
Mueller, W.E.G., 0174
Muensch, H., 0636, 0637
Mufson, M.A., 1546
Mulcahy, R., 0297-0301
Mulchi, C.L., 1028, 1030
Mullen, J.B.M., 0101
Mullen, P., 0646
Muller, J., 0097
Mulligan, J.J., 1082
Mun, J.Y., 0443
Munster, M., 1332
Mur, J.M., 0221, 0224, 0244
Murad, F., 0740
Muramatsu, S., 0353
Muramatsu, T., 0353
Muranaka, H., 0375
Murdia, U.S., 0266
Murphy, R., 0978
Murray, A.B., 0076
Murray, D.M., 1131-1133
Murray, J., 1458
Murray, J.F., 0651
Murty, K.P.S.N., 0267
Mushinski, M., 1243
Musy, C., 0479
Myers, H., 0102
Myhre, B.A., 0958, 0963
Myles, W.S., 0078
Mylius, E., 0421, 0422

Nadler, J.L., 0668
Naeraa, N., 0166
Naeye, R.L., 1391
Nagai, M., 0360
Nagashima, T., 0363
Nagpaul, K.K., 0273
Nair, J., 0266
Nakagawa, N., 0352
Nakamura, M., 0355, 0389
Nakayama, T., 0385
Nandrup, S., 0169
Narula, J., 0285
Nasca, P.C., 1254, 1256
Nasiell, M., 0462
Ndhlovu, R., 1563
Needle, R.H., 1134
Neittaanmaki, L., 0205
Nemoto, N., 0354
Nemtzov, A.A., 0501
Nerenz, D.R., 1558
Nery, L.E., 0060
Neukirch, F., 0226, 0234, 0236, 0497
Newhouse, M.L., 0565
Newman, I.M., 1161
Newman, M.J., 0982
Newman, N., 0045
Newman, R.C., 1556
Ngo, E., 0642
Nichols, B.C., 1451
Nichoman, M.Z., 1480
Nickerson, C.J., 1516
Niebuhr, E., 1579, 1580
Niederman, M.S., 1249
Nielsen, M.T., 0911
Niemensivu, H., 0201
Nikodemowicz, E., 0427, 0428
Nil, R., 0481-0487
Nilsen, A., 0421
Nilsen, S.T., 0415
Nishikawa, Y., 0362
Nissinen, A., 0197
Niukian, K., 1058
Noble, E., 0135
Nogawa, A.N., 0650
Nolan, W.P., 0807
Nomura, A.M., 0829, 0832, 0833
Norell, S.F., 0467
Notani, P.N., 1581
Nourish, D.J., 0020
Nowak, J., 1458
Nutbeam, D., 0596, 0597
Nylund, L., 0449

O'Brien, D.E., 1466
O'Connell, K.A., 1142
O'Conner, K., 0567
O'Connor, J., 0295
O'Connor, K.P., 0530
O'Donohue, W.J., Jr., 1152
O'Neill, I., 0245, 0250
O'Neill, S., 0302
O'Shea, R.M., 1272, 1283
Oberle, M.W., 0811
Ochs, H.R., 1080
Ockene, J., 1083-1088, 1091
Odukoya, O., 1059
Oelman, B.J., 0539
Oesch, F., 0190
Offenbacher, S., 0819
Ogawa, H., 0350, 0351
Ohkubo, C., 0368-0372
Ohlson, C.-G., 0460
Okubo, T., 0391
Olinsky, A., 0022, 0023
Olofsson, J., 0457
Olsen, C., 0166
Olsen, J., 0161
Olson, W.K., 1174
Omar, S., 0173
Omenn, G.S., 1530, 1531
Onadeko, B.O., 0406
Onadeko, M.O., 0406
Orchard, T.T., 1417
Orlandi, M.A., 1213
Orleans, C.T., 1322
Osawa, Y., 1240
Osman, M., 1226
Ossip-Klein, D.J., 1271, 1289
Oster, G., 1079
Osterdahl, B.-G., 0466
Ostrow, D.G., 0837
Otradovec, K., 1143
Ounsted, M., 0573
Overton, D.A., 1406
Owen, N., 0030
Owen, P., 0017
Owens, M., 1364
Owsinski, J.M., 0426-0428

Padmanabhan, R., 1117
Pain, M.C.F., 0022
Palat, M., 0152
Pallonen, U., 0200
Palmer, R.D., 1149
Pan, X.W., 0146, 0147
Panciera, T., 1436
Pandey, M.R., 0393
Panella, V., 0341
Panemangalore, M., 0885
Papier, C., 0315
Parcel, G., 1476
Park, K.H., 0441, 0443
Park, S.S., 0990
Parker, B.D., 1301

INDEX OF PRINCIPAL INVESTIGATORS

Parker, B.M., 1143
Pasanen, M., 0211, 0216
Passa, P., 0239
Pastore, G., 0317
Pastorino, U., 0326, 0327
Patel, D.D., 0270, 0271
Patel, R.D., 0269, 0271
Patel, T.B., 0269-0271
Paterson, D., 0135
Patois, E., 0225
Patten, B.M., 1463
Pavia, D., 0550, 0551
Pawlik, W.W., 1358
Pearson, J.C.G., 0569
Pearson, M.G., 0136
Peat, J.K., 0043, 0044
Pechacek, T., 1122, 1125
Pederson, L.L., 0130-0133, 0137, 0138
Peh, K.L., 0392
Pekurinen, M., 0199
Pelkonen, O., 0211, 0212, 0215
Penny, W.J., 0601
Perdrizet, S., 0226, 0232, 0233, 0235, 0240, 0497
Perera, D.R., 1537
Peritz, E., 0312
Perry, C., 1062, 1131, 1132, 1135
Perry, R.J., 1433, 1438
Pershagen, G., 0459
Persson, B., 0449
Pert, A., 0983
Pesonen, E., 0193
Peters, E.C., 1391
Peters, R.W., 1036
Petersen, M., 1543
Peterson, A.V., Jr., 1516, 1519
Petitti, D.B., 0641
Peto, J.T., 0508
Peto, R., 0547
Petrakis, N., 0711
Pham, Q.T., 0221-0223
Phelan, P.D., 0022
Philips, B.U., 1476, 1477
Phillips, G.T., 1464
Phillips, M.A., 0741
Phillips, R.E., 0927, 0953
Piascik, M.T., 0912
Pickens, R.W., 1118, 1125
Piechowski, J., 0242
Pierce, D.K., 1369
Pierce, J.A., 1148
Pierce, J.P., 0009
Pierre, F., 0224
Piha, T., 0201
Pike, M.C., 0731
Pillsbury, H.C., 0777
Pindborg, J.J., 0165, 0288
Pinder, J.E., III., 1443
Pinnas, J., 0621
Pirie, P., 1133
Pisani, P., 0320
Pisiewicz, K., 0435
Pistulkova, H., 0154
Pittilo, R.M., 0535-0538
Pitts, W.M., 1488
Placek, P., 0977
Platt, K.L., 0190
Plesec, T.L., 1349
Plomin, R., 0754
Plude, D.J., 1066
Pocock, S.J., 1602
Poe, R., 1271
Poggi, A., 0321
Poirier, M.C., 0984
Polen, M.R., 0643
Pollin, W., 0975
Pomerleau, O.F., 0767
Pool, J., 0556
Pope, M.H., 1500
Pories, W.J., 1311
Poulson, T.C., 0756
Powell, D.R., 1099-1101
Powell, K.E., 0813
Prada, J.A., 1014
Prasad, K.S.R., 0283
Prasad, V.H., 0283
Pratt, J.W., 0644
Pratt, L., 1512
Pratt, W., 0981
Preber, H., 0455
Prescott, R.J., 0600
Preston-Martin, S., 0245, 0720, 0721, 0733
Prichard, J.S., 0302
Pride, N.B., 0514
Prochaska, J.O., 1434, 1435
Prokhorov, A.V., 0502
Prokopczyk, B., 1196
Proust, J., 0218
Prue, D.M., 1139
Pryor, W.A., 0961
Pulkkinen, P., 0213
Pullella, J.L., 1341
Puska, P., 0197, 0198, 0200, 0201

Quan, S., 0620
Quintero Gonzalez, J., 0150

Rabkin, S.W., 0118, 0119
Rachootin, P., 0161
Radhakrishnamurthy, B., 0962
Raghu, G., 1538
Ragland, D.R., 0676
Raguso, E., 0329
Rahim, M.A., 0051, 0052
Raia, T., 1083, 1084
Rajani, S.P.C., 0270
Rajaniemi, H., 0212
Rama Sastry, B.V., 1454-1456
Ramirez, A., 1481
Randerath, K., 1460
Rankin, D.W., 0010, 0011
Rao, G.S., 1117
Rao, S.A., 0283
Rauramaa, R., 0204
Ravenholt, R.T., 0971, 0975
Raw, M., 0553, 0554
Ray, R.L., 0996
Rayford, P.L., 0627, 0628
Read, R.C., 0630, 0631
Reavill, C., 0520
Redman, S., 1568, 1570
Reduzzi, D., 0319
Reed, E., 0984
Reed, R.N., 1489
Rehm, S.R., 0906-0908, 0913
Reid, A.L.A., 1568, 1569
Reidenberg, M.M., 1413
Reif, A.E., 1042
Reith, M.E.A., 1250-1252
Renaud, S., 0229, 0230
Renzi, G.D., 0095
Renzi, P.M., 0094, 0095
Repace, J.L., 0783
Repine, J.E., 0759
Resnik, R., 0671
Reynolds, H.Y., 0768, 0769
Rice, D.A., 0965
Richards, I.P.D., 0510
Richardson, D., 0904, 0914, 0955
Richardson, R.R., 1362
Richmond, R.L., 0037, 0038
Richter, A., 0110-0112, 0114, 0115
Richwald, G., 0634
Riebsame, W., 1513
Rieck, C.E., 0927
Rigatto, M., 1573
Rigotti, N., 1074
Rimer, B.K., 1386
Rippe, J., 1086, 1088
Rippe, J., 1088
Risner, M.E., 1013, 1014
Rivedal, E., 0412
Rizzi, M., 0329
Robins, A.G., 1165
Robinson, K., 0014
Robinson, K.R., 0035
Roels, H., 0056
Rogan, E.G., 1159
Roger, V., 0462
Rogers, A.W., 0575
Rogers, R.L., 1484-1487
Rogers, R.M., 1127
Rogers, W.R., 1467
Rogot, E., 1011
Rojanetz, R.V., 0501
Rokaw, S., 0682
Rokeach, M., 1541
Romanski, B., 1594
Romig, P.L., 1178, 1180
Roscoe, R., 1350
Rose, E.F., 0445
Rose, J.E., 0693, 0694, 0736, 0737
Rosecrans, J.A., 1514
Rosen, M.A., 1242
Rosenberg, J., 0413
Rosenberg, L., 1039, 1040

INDEX OF PRINCIPAL INVESTIGATORS

Rosenman, R.H., 0655, 0676
Rosero, L., 0811
Rosin, M.P., 0064, 0065
Rosner, B., 1053, 1054
Ross, R.E., 1175
Rosser, W.W., 0120, 0121
Rossman, M.D., 1415
Rossman, T.G., 1258
Rosti, J., 0202
Roth, W., 1280
Rothenberger, L.A., 1325
Rowell, P.P., 0941
Rubin, G., 0812
Rubinson, L., 0851
Rudnik, J., 0435
Rudolph, A.M., 0672
Ruehlman, P., 1351
Rufty, T.W., 1329
Rush, B.F., 1182, 1185
Rush, D., 1192, 1229
Russell, M., 1265, 1266
Russell, M.A.H., 0522, 0557
Rutten, A.A.J.J.L., 0395
Ryan, A.J., 1571
Rylander, R., 0475

Saccomanno, G., 0764
Sachs, D.P., 0739
Sachs, D.P.L., 1348, 1355
Sackner, M.A., 0791, 0792
Sadur, C.N., 0762
Sagen, N., 0415
Said, G., 0225
Sainte-Laudy, J., 0247
Sakai, T., 0383
Sakuma, H., 0374
Salomaa, S., 0195
Salonen, J.T., 0204
Saloojee, Y., 0552
Salvaggio, J., 0966
Samet, J.M., 1189-1191
Samis, H.V., Jr., 0800
Sampol, J., 0220
Sancho Garnier, H., 0231
Sandell, J., 0263
Sanders, D., 0548, 0570
Sanders, L., 1366
Sandler, D.P., 1313, 1314
Sandoval, P.R.M., 0060
Sanner, T., 0412
Sannita, W.G., 0324
Sano, F., 0391
Sanson-Fisher, R.W., 1568, 1570
Santella, R., 1230
Santi, L., 0334, 0336
Sappenfield, W.M., 0809
Saracci, R., 0245
Sarna, S., 0193
Sasaki, M., 0389
Sasaki, R., 0384
Sati, T.R., 0263
Sato, T., 0349
Sattin, D., 0970
Saunders, J.A., 1034
Saunders, M., 0540
Savino, A., 0343
Sawada, H., 0359
Sawada, M., 0386
Sayed, A.R., 0447
Scalliet, D., 0478
Scassellati Sforzolini, G., 0343
Schaps, E., 0647
Schar, M., 0490
Schechter, F.G., 0106
Scheinberg, I.H., 1303
Schelling, T.C., 1068, 1069
Schenker, M.B., 0677
Schepartz, A.L., 0804
Schievelbein, H., 0183
Schimpfhauser, F.T., 1272, 1283
Schindl, R., 0049
Schinke, S.P., 1527, 1532, 1533
Schleiter, M., 0697
Schlesinger, P., 0856
Schlesinger, R.B., 1260
Schlosser, K., 0181
Schlotzhauser, W.S., 0806, 1321
Schmahl, D., 0175
Schmidt, F., 0188, 0189
Schneider, A. W., 0792
Schneider, N.G., 0681, 0683
Schneider, S.J., 1220, 1237, 1302
Schnell, A., 0139, 0140
Schoeller, D.A., 0848
Schoenbach, V.J., 1322
Schoenberg, J., 1172
Schoeneman, T.J., 1368
Schonheyder, H., 1577
Schroll, M., 0168
Schubert, D.K., 0735
Schuler, G., 0495
Schuntermann, M.F., 0191
Schuurman, J.H., 0397
Schwartz, D., 0227
Schwartz, J.L., 0639
Schwartz, S.M., 1522
Sciandra, R., 1268
Scott, A., 0573
Scott, K.E., 0077
Seaborn, J., 0063
Secker-Walker, R.H., 1501-1504
Seedat, H.A., 0446
Seffrin, J.R., 0859
Sell, A., 0164
Selvester, R.H., 0649
Semmence, A., 0533
Sergi, M., 0328, 0329
Serlin, O., 1185
Sershen, H., 1250-1252
Severson, H.H., 1373
Severson, R.F., 0821
Sexton, M., 1022
Seydewitz, V., 0184
Shader, R.I., 1080
Shakotko, R., 1176
Shamarin, V M., 0503
Shaper, A.G., 1602
Shapiro, S., 1039, 1040
Sharma, P.K., 0273
Sharma, P.L., 0282
Sharp, J., 0858
Shaver, M., 0186, 0187
Shaw, J.G., 0931, 0933
Shaw, T.S., 0788
Shean, R.E., 0006
Sheen, S.J., 0891
Shekelle, R.B., 1480
Shephard, R.J., 0126
Shepherd, P.L., 0789, 0790
Sherman, L., 1372
Sherrard, D., 1534
Shertzer, H.G., 1360
Shibata, A., 1590
Shiffman, S., 0799, 1420
Shiga, M., 0359
Shionoya, S., 0384
Shipley, R.H., 1334-1337
Shirodkar, V. B., 0293
Shklar, G., 1058, 1059
Shoch, P., 1249
Shopland, D.R., 0972-0974
Sidney, S., 0641
Sieber, M.F., 0494
Sieffert, G.F., 0745
Sigman, G., 1609
Silman, A., 0528
Silva, P., 1592
Silver, K.J., 1348, 1355
Silverman, D., 1010
Silverman, F., 0126
Silverman, S., Jr., 0702, 0714, 0715
Silverstein, M.D., 0849
Simmons, R.A., 0634
Simms, J.L., 0921
Simms, M., 0517
Simpson, F.O., 0405
Sims, J.L., 0920, 0921, 0926, 0944-0946
Sindberg-Eriksen, P., 0469
Sinkiewicz, W., 1594
Sirota, A.D., 1436, 1439-1441
Sisson, V.A., 1331
Sjostrand, M., 0475
Skipper, P.L., 1077
Skoog, H.A., 1033
Slade, J.D., 1173
Sleight, P., 0547
Sloan, J.S., 0910
Slorach, S.A., 0466
Sly, P.D., 0023
Smith, C., 0517
Smith, M., 1457
Smith, M.S., 0951
Smith, T.J., 1076
Smith, W.C., 0582, 0583
Smithbauer, W.G., 1170
Snider, G., 1364
Snider, G.L., 1044

INDEX OF PRINCIPAL INVESTIGATORS

Snook, M.E., 0822
Sober, A.J., 1073
Sofalvi, A.J., 0845
Sofuni, T., 0386
Sokol, R.J., 1344
Solomon, R., 1437
Soloway, R., 1414
Solt, D.B., 0841
Somers, K.D., 1507
Sommer, A., 0999
Song, B.J., 0990
Sonnenfeld, G., 0939
Sontag, S.J. 0857
Sopori, M., 0915
Sorenson, J., 1038
Sorsa, M., 0194, 0195
Sotaniemi, E.A., 0215
Southwood, D.M., 1564
Sparacino, C.M., 1320
Sparrow, D., 1096
Spealman, R.D., 1055, 1057
Speizer, F.E., 1063, 1078
Spira, A., 0227
Sprince, H., 1428
Springmeyer, S., 1538
Spritz, H., 1299
Spruill, W.M., 1033
Spurr, H.W., Jr., 0947, 1304
Squier, C.A., 0875
Staessen, J., 0056
Staguhn, M., 0182
Stale, H., 0469
Stallones, R., 1472
Stamford, B.A., 0934, 0942
Stampfer, M., 1054
Stanish, W., 1490
Stark, R., 1228, 1231
Starzyk, P.M., 1521
Staubesand, J., 0184
Staun, P., 0159
Steffen, R., 0490, 0491
Steffens, G.L., 1292
Stein, Z., 1257
Steiner, R.P., 0940
Stemhagen, A., 1172
Stenhouse, N.S., 0008
Stephen, A.M., 0533
Stephenson, M.G., 0826
Stephenson, W.P., 1091
Sterboul, J., 0247
Sterling, E.M., 0099, 0100
Sterling, T.D., 0099, 0100
Stern, M., 1481
Stetson, D.E., 1302
Stevens, J.B., 1121
Stevens, K.Y., 0011
Stevens, V.J., 1367
Stewart, P.J., 0120
Stewart, S., 1512
Stich, H.F., 0064-0066
Stitzer, M.L., 1008
Stokes, J., III., 0987, 1041
Stolerman, I.P., 0520, 0521
Stolley, P.D., 1413, 1414
Stone, P.J., 1044, 1048
Stookey, G.K., 0861
Stoto, M.A., 1070
Stott, H., 0508
Strecher, V.J., 1106, 1386
Strehler, C., 0217
Strickland, C., 0132
Strom, B.L., 1413, 1414
Strong, D.B., 1361
Stroup, N., 0812
Strub, H., 0217
Strum, B., 1395
Stueber, J.J., 0178
Sturmans, F., 0397
Suarez, L., 0701
Sudan, B.J.L., 0217, 0247
Sue, D.Y., 0640
Suedfeld, P., 0109
Sugawara, S., 0374
Summer, D.A., 1319
Summy-Long, J.Y., 1392
Suranyi, G., 0097
Surawy, C.J., 0561
Surman, O.S., 1075
Susser, M., 1257
Sutton, S.R., 0504
Suzuki, S., 0391
Svardsudd, K., 0471, 0472
Svendsen, E., 0170
Svensson, C., 0459
Swan, G.E., 0655
Sweetnam, P.M., 0598
Swenson, I., 1326
Syndulko, K., 0744
Synkewecz, C.A., 1382
Szapocznik, J., 0797

Taber, L.H., 1462
Tai, H.-H., 0918, 0919
Takayama, S., 0354
Takeyama, H.F., 1153
Takishima, T., 0389
Talbot, R.W., 0104
Talbott, E., 1418
Taller, S.L., 0644
Talley, P., 1457
Tamir, A., 0305-0407
Tanaka, S., 0361
Tanaka, T., 0353
Tanida, T., 0375
Tannenbaum, G., 0316
Tannenbaum, S.R., 1077
Tannenbaum, T.N., 1087
Tanpairoj, S., 0498
Taraba, J.L., 0947
Tashkin, D., 0682, 0689
Tata, P.R., 0579
Tauchi, H., 0349
Taylor, C.B., 0654, 0659, 0663, 0664
Taylor, D.H., 0576
Taylor, H., 1396
Taylor, J.C., 0635
Taylor, R., 0047
Taylor, R.F., 0892
Taylor, R.T., 0893
Techlescu, D., 0221-0223
Teders, S.J., 1300
Telch, M.J., 0662
Telepchak, J.M., 0786
Temple, W., 1381
Tennant, F.S., Jr., 0638
Terracini, B., 0344-0347, 1183
Tewar, M., 1582
Thelin, A., 0465
Thelle, D., 0420
Theriault, G., 0086, 0087
Thier, H.D., 0675
Thomas, D.B., 1520
Thomas, H.E., 1045
Thomford, P., 0626
Thompson, J.A., 0760
Thompson, M.E., 0128
Thompson, W.D., 0770
Thorn, J., 0163
Thornton, J.C., 0722, 0723
Thurmer, H., 0410
Thurston, R., 0948
Tian, P.S., 1592
Timisjarvi, J., 0210
Timofeeva, S.G., 0503
Tipton, R., 1513
Tirlapur, V.G., 0602
Tirmarche, M., 0242
Tobin, M.J., 0791, 0792
Tockman, M.S., 0997, 1005-1007
Tokudome, S., 0388, 0390
Tolan, G.D., 1465
Toledo, L., 0139, 0140
Tolsma, D., 0814
Tominaga, S., 0257, 0350, 0352
Tooley, J., 1220
Tos, M., 0160
Touitou, Y., 0218
Townley, R.G., 1153
Townsend, J., 0542, 0543
Townsend, M.C., 1419
Travis, J., 0825
Trebbin, W.M., 1433, 1437, 1438
Tremblay, C., 0087
Trevor, A.J., 0708
Trichopoulos, D., 0254-0256
Trivers, G., 0216
Tso, T.C., 0603, 0932, 1034, 1238
Tsuchiya, E., 0257
Tsuchiya, Y., 1357
Tsuda, S., 0367
Tuimala, R., 0213
Tunstall-Pedoe, H., 0582, 0583
Tuomilehto, J., 0197
Turker, R.K., 0500
Turner, J.W., 1037
Tuyns, A., 0347
Tyagi, N.K., 0292

INDEX OF PRINCIPAL INVESTIGATORS

Tyler, C.W., 0812
Tzannes, S., 0255

Uebori, M., 0361
Ulmansky, M., 1282
Ulmer, W.T., 0181, 0182
Ulrich, M., 0162
Umeda, H., 0363
Uotila, P., 0214
Uppal, R., 0282
Urberg, K., 1112, 1113
Urch, B., 0126
Urso, P., 0820

Vahakangas, K., 0211, 0212, 0215, 0216, 0982
Vale, A., 0587
Valente, 0326
Van der Hoeven, J.C.M., 0394
Van Oostdam, J., 0108
Van Rensburg, S.J., 0445
Van Vunakis, H., 1049, 1050
Van Wyk, C.W., 0446
Vandeberg, J., 0865
Vandewiele, M., 0055
Vandongen, R., 0047
Vanuxem, D., 0220
Vartiainen, E., 0200
Vaughan, T.L., 1518, 1520
Velve Byre, K., 0414
Ventrone, R., 0479
Ventura, M.R., 1294
Verble, S.D., 1445
Vermeulen, A., 0054, 0399
Vessey, M., 0571, 0572
Vestal, R.E., 0834
Vicary, J.R., 1393, 1394
Vidic, B., 0778
Vineis, P., 0344
Vinitski, S., 0136
Vlietstra, R.E., 1116
Voelz, G.L., 1187
Vokonas, P.S., 1046
Von Gernet, A.D., 0085
Vorgia-Dalla, P., 0253
Vredevoe, D.L., 0687
Vutuc, C., 0050

Wabrek, A.J., 0765
Waddell, W.J., 0935, 0936
Wadsworth, M.E.J., 0560
Wagner, E.H., 1322
Wagner, G.J., 0916
Wakefield, M., 0024
Walaszek, A., 1354
Wald, N.J., 0533, 0534
Walker, A.M., 0246
Walker, D.C., 0108
Wallston, K.A., 1457
Walsh, D.C., 1047
Walter, H.J., 1214
Walton, L.R., 0925, 0952
Wang, N.-S., 0088
Wang, R., 0148, 0149
Wangensteen, O.D., 1119
Warburton, D.M., 0574
Warheit, G.J., 0796
Waring, W., 0965
Warmack, D., 0957
Warnecke, R.B., 0855
Warshaw, J.E., 0772
Warshaw, R., 0722, 0723
Watanabe, M., 0575
Watson, L., 0032-0034, 0036
Watts, J.R., 1443
Weathers, D.R., 0819
Webb, R.E., 1510
Webb, T.E., 1354
Webster, I.W., 0037, 0038
Weeks, W.W., 1330
Weerapradist, W., 0498
Weidner, G., 1277
Weinbaum, G., 1407
Weinberger, M.M., 0869, 0870
Weinstein, I.B., 1227
Weiss, S.T., 1096
Weiss, W., 1388-1390
Welch, Q.B., 1141
Welin, L., 0472
Weller, 0195
Wells, K.B., 0697
Welte, J.W., 1265
Wenke, G., 1196
Wennmalm, A., 0452
Wentz, R., 1338
Wesnes, K., 0574
West, D.W., 1490
West, R., 0522
Wewers, M.E., 1031
Wheeler, L.A., 0743
Whisnant, J.P., 1115
White, C.C., 0810, 0814
White, C., 0813
White, J.M., 1567
White, R., 0480
Whittemore, A.S., 0656, 0661
Whyte, H.M., 0021
Wicken, A.J., 0519
Widimsky, J., 0154
Wiggs, L.D., 1187
Wiio, J., 0198
Wiist, W., 1364
Wilber, C.G., 0750, 0751
Wilcox, A.J., 1313
Wilcox, B., 1601
Wilhelmsen, L., 0471, 0473, 0474
Wilkins, J.N., 0746
Wilkinson, G.S., 1187
Willan, A. R., 0070
Willcox, S., 0005
Willett, W., 1053
Williams, D.G., 0579
Williams, J., 1088
Williams, M.D., 1409
Williams, R.B., 1305
Williams, T., 0625
Williamson, R.E., 1321, 1329
Wills, R., 0776
Wilmer, J.W.G.M., 0395
Wilner, S., 0713
Wilson, D., 0024
Wilson, D.M.C., 0089, 0129
Wilson, J.A., 0580
Wilson, R.W., 0956
Wilson, S.E., 0742
Wimmer, H., 0835
Wincze, J.P., 1439, 1440
Windsor, R.A., 0607
Wingard, D., 0698
Winters, A., 0609
Winters, T.H., 1092
Witten, M., 0620
Wojcieszek, Z., 0432
Wojcik, J., 1114
Wolf, J., 1293
Wolfe, G., 0747
Wolfe, W.G., 1333
Wolk, A.W., 1344
Wong, F., 0815
Wood, Y., 1162
Woodson, P.P., 0483, 0485, 0487
Woodward, A., 0025, 0029, 0030
Woodward, S.D., 0020
Woolcock, A.J., 0043, 0044
Wooley, B., 1176
Woolf, N., 0535, 0536, 0538
Woolman, P., 0506
Worden, J.K., 1501, 1503
Wright, E.C., 1006
Wright, J.L., 0101
Wu, A.H., 0730, 0731
Wulf, H.C., 1579, 1580
Wurtz, J., 0049
Wyatt, J.R., 1459
Wyatt, R.J., 0906, 0907
Wynder, E.L., 1215, 1216, 1299
Wysocki, M., 0434

Yacullo, M.A., 1270
Yamaguchi, H., 1093
Yamamoto, H., 0365
Yamamoto, J., 1102
Yanagawa, H., 0360
Yanagita, T., 0356, 0357
Yang, S.K., 1018
Yano, K., 0828
Yarnell, J.W.G., 0598
Yasko, J.M., 1422
Yates, A.J., 0046
Yoder, E.E., 0882, 0884, 0928, 0947, 0949
Yoo, K.-K., 0442
Yost, T.J., 0762
Young, D., 1294

INDEX OF PRINCIPAL INVESTIGATORS

Young, M., 0625
Yu, M.C., 0721, 0730, 0732
Yuan, G.X., 0144
Yuspa, S.H., 0984

Zahavi, I., 0309
Zahn, R.K., 0174, 0178
Zamel, N., 0125
Zanzari, P., 1586
Zatonski, W., 1595-1589
Zavala, C., 0141
Zawadzka, S., 0426
Zbikowska, M., 1594
Zeller, W.J., 0175
Zemla, B., 0432
Zengil, H., 0500
Ziolo, H., 0436
Zoller, U., 0310, 0311
Zuckerman, B.S., 1038

INDEX OF ORGANIZATIONS

Aalborg Regional Hospital, 0156
Academic Hospital, 0054
Academy of Science and Literature, 0174
Action on Smoking and Health, United Kingdom, 0505
Addenbrooke's Hospital, 0506
Addiction Research Foundation, 0061, 0496
Agia Sophia Children's Hospital,
  Institute of Child Health, 0251
Agricultural University, 0394
Agriculture Canada, 0062
Aichi Cancer Center Hospital, 0349
Aichi Cancer Center Research Institute, 0350-0352
Aichi Medical University,
  Institute for Medical Science of Aging, 0349
Aichi University of Education, 0353
Albert Einstein College of Medicine, 1192
Alberta Inter-Agency Council on Smoking and Health (Calgary Chapter),
  Tom Baker Cancer Centre, 0063
All-Union Cardiological Research Center, 0501
Allegheny County Health Department, 1382
Allegheny County Health Department,
  Bureau of Health Education, 1383
Amberley Associates, 1342
American Cancer Society, 1193-1195
American Council for an Energy-Efficient Economy, 0775
American Health Foundation, 1213, 1214, 1216
  Naylor Dana Institute, 0250, 1196-1212, 1215, 1253
American Heart Association,
  Oregon Affiliate, 1366
American Institute for Preventive Medicine, 1099-1101
American Lung Association, 1218, 1219
American Lung Association of DuPage and McHenry Counties, 0835
American Lung Association of Los Angeles County, 0634
American Lung Association of Mid-New York, 1217
Ankara Nuclear Research and Training Center, 0499
Anti-Cancer Council of Victoria, 0003-0005
Association Departementale d'Education Sanitaire et Sociale de l'Isere, 0478
Auburn University, 0604
Augusta Veterans Administration Medical Center, 0807
Australian Council on Smoking and Health, 0006
Australian Government Analytical Laboratories, 0007

B.R.D. Medical College, 0263
Bangladesh Cancer Epidemiology Research Program, 0051
Battelle, Geneva Research Center, 0479, 0480
Battelle, Pacific Northwest Laboratories, 1515
Baylor College of Medicine, 1460, 1461, 1463
  Influenza Research Center, 1462
Baystate Medical Center, 1037
Beaver College, 1384
Behavioral Health Systems, 1220
Ben-Gurion University of the Negev, 0304
Beth Israel Hospital, 1166
Biofeedback Laboratory, 0787
BIOSPEC, Inc., 1429
Boston City Hospital, 1038
Boston University, 1039-1048
Bowling Green State University,
  Electron Microscopy Center, 1343
Brandeis University, 1049, 1050
Brigham and Women's Hospital, 1051
British Broadcasting Corporation, 0507
British Columbia Cancer Research Centre,
  Environmental Carcinogenesis Unit, 0064, 0065, 0066
British Thoracic Society, 0594
  Sully Hospital, 0593
Brompton Hospital,
  Medical Research Council, 0508
Brookhaven National Laboratory,
  Medical Research Center, 1221
Brown University,
  Memorial Hospital, 1430
  Miriam Hospital, 1431, 1432
Budapest Bajcsy-Zsilinszky Hospital,
  Tuberculosis Institute, 0260
Bureau of Tobacco Control and Biometrics, 006

Cairo University,
  Cancer Institute, 0173
Calcutta University,
  University College of Science, 0264, 0265
California School of Professional Psychology, 1114
Canadian Department of National Health and Welfare,
  Medical Service Branch, 0068
Canadian Heart Foundation, 0069
Cancer Control Agency of British Columbia, 0070
Cancer Epidemiology Research Program, 0052
Cancer Institute, 0354
Cancer Research Institute,
  Carcinogenesis Division, 0266
Cancer Research Institute, Tokyo,
  Institute of Radiology and Oncology, 0257
Cancer Society of New Zealand, Inc., 0403
Cardiff Royal Infirmary, 0595
Cardiothoracic Institute at Midhurst, 0509
Carle Clinic Association Wellness Center, 0836
Carleton University, 0071-0073
Carmel Hospital,
  Faculty of Medicine, 0305-0307
Carnegie-Mellon University, 1385
Carter-Unicoi-Johnson Health Districts, 1445
Case Western Reserve University,
  Cleveland Metropolitan General Hospital, 1344, 1345
Case Western Reserve University,
  School of Dentistry, 1348
Case Western Reserve University,
  School of Medicine, 1346, 1347
Cattedra di Epidemiologia dei Tumori, 0317
Center for Adult Diseases, Osaka, 0355
Central Institute for Experimental Animals, 0356, 0357

References following all entries are to Description Numbers.

INDEX OF ORGANIZATIONS

- Central Tobacco Research Institute, 0267, 0268
- Centretown Community Health Centre, 0074
- Centro de Investigaciones Toxicologicas,
  - CITEFA/CONICET, 0001
- Chaim Sheba Medical Center, 0308
- Charles Camsell General Hospital,
  - Faculty of Medicine, 0075
- Charles University, 0151
- Chiba University,
  - School of Medicine, 0358
- Children's Heart Institute of South Texas, 1464
- Children's Hospital Medical Center, 1052
- Childrens Hospital of Vancouver, 0076
- CigaRest Quit-Smoking Center, 0788
- City of Hope National Medical Center, 0635-0637
- City University of New York,
  - Mount Sinai School of Medicine, 1222, 1223
- Clemson University, 1442
- Cleveland Clinic Foundation, 1349
- Colorado State University, 0750, 0751
- Columbia University, 1229, 1230
    - College of Physicians and Surgeons, 1224, 1226, 1228, 1231
    - School of Public Health, 1225, 1227, 1232
- Community Health Projects, Inc., 0638
- Community Mental Health Service, 1167
- Cookridge Hospital,
  - Yorkshire Regional Cancer Organization, 0510
- Copernicus Academy of Medicine, 0426-0428
- Cornell University,
  - School of Medicine, 1233-1235
- Creighton University,
  - Allergic Disease Center, 1153
    - School of Medicine, 1152
- Custom Supplements, Inc., 1236

- Daicel Chemical Industries Ltd., 0359
- Dalhousie University,
  - Community Reproductive Care Program, 0077
- Darlington Memorial Hospital, 0511
- Dartmouth College,
  - Dartmouth Medical School, 1163, 1164
- Defence and Civil Institute of Environmental Medicine, 0078
- Derer's Hospital,
  - Postgraduate Medical School, 0152
- Deutsches Krebsforschungszentrum,
  - Institute of Toxikologie und Chemotherapie, 0175
- District Institute of National Health,
  - Chest Clinic, 0153
- Dubuque Emphysema and Bronchitis Foundation, 0364
- Duke University Medical Center, 1305-1310
- Dundee University,
  - Ninewells Hospital and Medical School, 0580

- E.I. du Pont de Nemours and Company, 0786
- East Carolina University,
  - School of Medicine, 1311
- East Tennessee State University,
  - College of Medicine, 1446
- Eastern Virginia Medical School, 1507
- Ecole Nationale Superieure de Chimie, 0217
- Ecole Normale Superieure, Un. Dakar, 0055
- Economic and Social Research Institute, 0294
- Economic Research Service, 0776
- Elisabethinen Hospital Linz, 0049
- Emory University,
  - School of Dentistry, 0819
    - School of Medicine, 0818
    - Yerkes Regional Primate Research Center, 0817
- Environmental Pollution Control Center, 0361, 0362
- Escola Paulista de Medicina,
  - Laboratorio Fleury, 0060
- Escuela Nacional de Educacion Tecnica No. 5, 0002
- Evangelismos Hospital Medical Center, 0252

- Faculte de Med Pitie-Salpetriere, 0218
- Faculty of Medicine of Lisbon, 0439, 0440
- Federal Trade Commission,
  - Tobacco Research Laboratory, 0777
- Fibiger Institute,
  - Laboratory of Environmental Carcinogenesis, 0157, 0158
- Florida International University, 0789, 0790
- Foundation for Blood Research, 0969
- Fox Chase Cancer Center, 1386, 1387
- Francis Scott Key Medical Center, 0991, 0992
- Franklin Institute, 1016, 1017
- Fred Hutchinson Cancer Research Center, 1516, 1518-1520
    - Swedish Hospital Tumor Institute, 1517
- Frederikssund Hospital, 0159
- Friarage Hospital, 0512
- Fujita-Gakuen Health University,
  - College of Medical Technology, 0363

- G.P. Pant Hospitals, 0274
- General Hospital of Monfalcone, 0318
- Gentofte University Hospital, 0160
- Georgetown University, 0780
    - School of Medicine, 0778, 0779
- Gippsland Institute of Advanced Education, 0079
- Glasgow University,
  - Ruchill Hospital, 0581
- Golda Medical Center, 0309
- Graduate Hospital,
  - Research Division, 1407
- Group Health Associates, 1351
- GSF Research Center, 0176, 0177
- Gujarat Cancer and Research Institute, 0269-0272
- Guy's Hospital Medical School, 0513

- Hahnemann University,
  - School of Medicine, 1388-1390
- Haifa University,
  - Oranim School of Education of the Kibbutz Movement, 0310, 0311
- Hammersmith Hospital,
  - Royal Postgraduate Medical School, 0514
- Harbor-UCLA Medical Center, 0640
- Hartford Hospital, 0765
- Harvard Medical School, 1055
    - Alcohol and Drug Abuse Research Center, 1056

INDEX OF ORGANIZATIONS

Harvard Medical School.
  Brigham and Women's Hospital, 1053, 1054
    New England Regional Primate Research Center, 1057
    John F. Kennedy School of Government, 1068-1070
    School of Dental Medicine, 1058, 1059, 1064
    School of Public Health, 0256, 1060-1063, 1067
    Veteran's Administration Outpatient Clinic, 1065, 1066
Health and Safety Executive, 0515
Health and Welfare Canada, 0080
Health Care Studies and Clinical Investigation Activity, 1466
Health Commission of Victoria, 0010, 0011
Health Department of Western Australia,
  Health Promotion Services, 0012-0015
Health Promotion Directorate, 0081-0083
Health Research Inc., 1238
Heartbeat Wales, 0596, 0597
Hebrew University,
  School of Public Health and Community Medicine, 0312
Helsinki University, 0193
Helsinki University Central Hospital, 0192
Herefordshire Health Authority, 0516
Hokkaido University,
  Research Institute of Applied Electricity, 0364
    School of Medicine, 0365, 0366
Hopital du Sacre-Coeur, 0084
Hopital Henri Mondor, 0219
Hopital Salvator,
  Laboratoire d'Explorations Fonctionnelles Respiratoires, 0220
Hospital Del Salvador, 0139
Hospital of Monfalcone, 0348
Howard University, 0782
Howard University Cancer Center, 0781
Huddinge University Hospital, 0449, 0450, 0451, 0452

Indiana University, 0859
    Center for Health and Safety Studies, 0860
    School of Dentistry and School of Medicine, 0861
INSERM, 0231-0239
INSERM Unit 14, 0221-0227, 0229, 0230, 0240, 0497
INSERM Unit 0228, 0287
Institut d'Etudes et Recherches Pneumophtisiologiques, 0241
Institut de Protection et de Surete Nucleaire, 0242
Institut National de Recherche et de Securite, 0243, 0244
Institut Territorial De Recherches Medicales Louis Malarde, 0497
Institute CIVO-Toxicology and Nutrition, 0395, 0396
Institute for Clinical and Experimental Medicine, 0154
Institute for Social Studies in Medical Care, 0517
Institute of Cancer Research, 0518, 0519
Institute of Community Health, 0161
Institute of Environmental Toxicology, 0367
Institute of Hygiene and Public Health, 0444
Institute of Immunology and Experimental Therapy, 0429, 0430
Institute of Internal Medicine, 0431
Institute of Occupational Health, 0194-0196
Institute of Oncology, 0432
Institute of Preventive Cardiology,
  Laboratory of Juvenile Hypertension, 0502, 0503
Institute of Psychiatry, 0520, 0521
    Addiction Research Unit, 0504, 0522
Institute of Public Health, Japan, 0368-0372
International Agency for Research on Cancer, 0245, 0246, 0250

Iowa Lutheran Hospital, 0865
Iowa State University, 0866, 0867, 0868
Istituto di Ricerche Farmacologiche "Mario Negri," 0321, 0322
Istituto Malattie Respiratorie Dell' Universita, 0323
Istituto Nazionale per la Ricerca sul Cancro, 0324, 0325
Istituto Nazionale Tumori, 0319, 0320, 0326, 0327

Japan Tobacco and Salt Public Corporation,
  Central Research Institute, 0373, 0374
    Kyoto Senbai Hospital, 0375
Jewish Hospital of St. Louis, 1140
Jichi Medical School, 0360, 0376
Johannes Gutenberg University,
  Academy of Science and Literature, 0178
John B. Pierce Foundation Laboratory, 0766
Johns Hopkins University, 0996, 1002
    Dana Center for Preventive Ophthalmology, 0999
    Francis Scott Key Medical Center, 1008
    School of Hygiene and Public Health, 0994, 0995, 0997, 0998, 1000, 1003, 1005-1007
    Training Center for Public Health Research, 1001
    Wilmer Ophthalmological Institute, 1004
Juntendo University,
  School of Medicine, 0377, 0378

K.V. Social Security SITE Hospital, 0424
Kaiser Foundation Research Institute, 0641, 0642
Kaiser-Permanente Center for Health Research, 1367
Kaiser-Permanente Medical Care Program, 0643
Kaiser-Permanente Medical Center, 0644
Kansas City, Missouri, Health Department, 1141
Kansas Department of Health and Environment, 0876
Karolinska Institute, 0453-0456
    Faculty of Odontology, 0455
Katholicke Universiteit van Leuven, 0056
Kaukini Medical Center, 0828
Kean College of New Jersey, 1168, 1169
Kentucky State University, 0885
Khyber Medical College, 0425
Kibbutz Gival Haim Ichud, 0313
King's College,
  School of Medicine and Dentistry, 0523
Kingston Polytechnic, 0524-0526
Klinik Loewenstein, 0179
Kobe University,
  School of Medicine, 0379
Komensky University, 0155
Korea Tobacco Research Institute, 0441-0443
Krakow Medical Academy,
  Institute of Social Medicine, 0433
Kurukshetra University, 0273
Kyoto University,
  School of Medicine, 0380

L. Sacco Hospital, 0329
    Servizio Fisiopatologia Respiratoria, 0328
Laboratoire d'Immunologie et d'Allergologie, 0247
Laboratory of the Government Chemist, 0527

INDEX OF ORGANIZATIONS

Labour Protection and Hygiene Centre,
  Laboratory of Cytology, 0444
Lahey Clinic Medical Center, 1071, 1072
Lega Italiana per la Lotta Contro i Tumori, 0330
Lenox Hill Hospital, 1239
Lewis and Clark College, 1368
Linkoping University,
  University Hospital, 0457
Loma Linda University,
  School of Health, 0645
London Hospital Medical School, 0528
London School of Hygiene and Tropical Medicine,
  TUC Centenary Institute of Occupational Health, 0529
London University,
  Institute of Psychiatry, 0530
Los Alamos National Laboratory, 1187
Louisiana State University, 0960, 0961
  National Research and Demonstration Center, Arteriosclerosis, 0959
  School of Medicine, 0958, 0962, 0963
Lund University,
  Health Sciences Center, 0458

Mahidol University,
  Faculty of Dentistry, 0498
Manchester Regional Committee for Cancer Education, 0531, 0532
Mario Negri Institute for Pharmacological Research, 0331, 0332
Marquette University,
  College of Nursing, 1547
Marshfield Clinic, 1548
Massachusetts General Hospital, 1073-1075
Massachusetts Institute of Technology, 1076, 1077
Maudsley Hospital,
  Smokers Clinic, 0557
Maulana Azad Medical College, 0274
Maxicare Research and Education Foundation, 0646
Mayo Foundation, 1115
Mayo Medical School, 1116
McGill University, 0085, 0088
  School of Occupational Health, 0086, 0087
McMaster University,
  Faculty of Health Sciences, 0089, 0129
Medical College of Oita, 0381, 0382
Medical College of St. Bartholomew's Hospital, 0533, 0534
Medical College of Wisconsin, 1549
Medical Control Centers, 1170
Medical Foundation of Buffalo, Inc., 1240
Medical Research Council, United Kingdom, 0598
Medical Research Council,
  Epidemiology and Medical Care Unit, 0541-0543
Medical Research Council,
  National Research Institute for Nutritional Diseases, 0445
Medizinische Universitats-Klinik, 0180
Memorial Hospital for Cancer and Allied Diseases, 1241
Metropolitan Life Insurance Co., 1242, 1243
Michigan Molecular Institute, 1102
Middle East Technical University, 0499
Middlesex Hospital, 0538
  Bland-Sutton Institute of Pathology, 0535-0537
Midwest Research Institute, 1142
Ministry of Defence, 0539
Ministry of Health and Ahfad College for Women, 0448
Mitsubishi Acetate Company Ltd., 0383
Montreal General Hospital, 0090
Morehouse School of Medicine, 0820
Moses H. Cone Memorial Hospital, 1312
Mount Sinai Medical Center, 0791, 0792, 1550
  Environmental Sciences Laboratory, 1244
Mount Sinai School of Medicine, 1245-1248
Mount Vernon Hospital,
  Regional Radiotherapy Centre, 0540
Mrigendra Medical Trust, 0393
Mumbwa District Hospital, 1563
Municipal Health Department, 0397

Nagoya University,
  School of Medicine, 0384
Nassau Hospital, 1249
Nathan S. Kline Institute,
  Center for Neurochemistry, 1250-1252
National Board of Electricity,
  Medical Service, 0333
National Cancer Center Research Institute, Japan, 0385
National Cancer Institute of Canada,
  University of Toronto, 0091-0093
National Center for Atmospheric Research, 0752
National Council on Smoking and Health, 0407-0410
National Heart Foundation of Australia, 0016
National Heart Foundation of New Zealand,
  Princess Margaret Hospital, 0404
National Institute of Environmental Medicine, 0459, 0467
National Institute of Hygiene, 0434
National Institute of Hygienic Sciences, 0386
National Institute of Public Health, 0387
National Institute on Cancer Research, 0334-0336
National Jewish Hospital and Research Center, 0753
National Mass Radiography Service, 0411
National Public Health Institute, Finland, 0197-0201
National Research Institute for Mother and Child, 0435
National University of Singapore,
  Kangang Kerbau Hospital for Women, 0392
New Addenbrooke's Hospital, 0544
New Jersey Medical School, 1171
New Jersey State Department of Health,
  Cancer Epidemiology Services Unit, 1172
New Mexico Institute of Mining and Technology, 1188
New York State Department of Health, 1254-1256
New York State Psychiatric Institute, 1257
New York University,
  School of Medicine, 1258-1261
Ninewells Hospital,
  Medical School, 0582-0584, 0587
North Carolina Agricultural and Technical State University,
  Tobacco and Pesticide Research, 1317
North Carolina State University, 1318, 1319
North Dakota State Department of Health, 1338
North Dakota State University,
  College of Pharmacy, 1340
    Oregon Research Institute, 1339
North Devon District Hospital, 0545
North Shore University Hospital, 1262

INDEX OF ORGANIZATIONS

Northeastern Ohio Universities,
  College of Medicine, 1352
Northwestern Memorial Hospital, 0837
Northwestern University, 0841
  Medical School, 0838
  Technological Institute, 0839. 0840
Northwick Park Hospital, 0546
Norwegian Radium Hospital, 0412
Notre-Dame Hospital, 0094
  Respiratory Service, 0095

Oak Ridge National Laboratory, 1447
Odense University Hospital, 0162
Ohio State University, 1353, 1354
Oklahoma State Department of Health,
  Health Education and Information Service, 1362
Ontario Ministry of Agriculture and Food,
  Pesticide Residue Testing Laboratory, 0062
Ontario Ministry of Labour, 0096, 0097
Oregon Health Sciences University, 1369, 1370
Oregon Research Institute, 1371-1373
Oslo Department of Health and Life Insurance Companies, 0414

Pennsylvania State University, 1393, 1394
  College of Medicine, 1391
  Hershey Medical Center, 1392
Peter Bent Brigham Hospital,
  Channing Laboratory, 1078
Philadelphia Department of Public Health, 1395
Pneumoconioses Research Institute, 0181, 0182
Policy Analysis Inc., 1079
Portland State University, 1374
Postgraduate Institute of Medical Education and Research, 0275-0282
Prevention Research Center, 1396
Prevention Research Center,
  Pacific Institute for Research and Evaluation, 0647, 0648
Prince Georges County Pubic Schools, 1015
Prince Henry Hospital, 0017
Process and Instruments Corporation, 1263, 1264
Provincial Blood Donation Centre and Provincial Union Hospital,
  0436, 0437
Puffability People, Inc., 0018, 0019
Pulmonary Associates, P.A., 0615
Purdue University, 0862

Queen Elizabeth Hospital, Hong Kong, 0257
Queen Elizabeth II Medical Centre, 0020
QUITS Smoking Cessation Service, 0021

Radcliffe Infirmary, 0547, 0548
Rancho Los Amigos Medical Center,
  Professional Staff Association, 0649
Regional Hospital, 0460, 0461
Research Dimensions, Inc., 1509
Research Group in Dental Epidemiology, 0446
Research Institute on Alcoholism, 1265, 1266
Research Laboratorie, 0183
Research Triangle Institute, 1320
Roger Williams General Hospital,
  Brown University Program in Medicine, 1433
Roswell Park Memorial Institute, 1267-1269
Royal Children's Hospital, 0022, 0023
Royal College of General Practitioners, 0549
Royal Dental College, 0163, 0288
Royal Free Hospital, 0550, 0551
Royal Gwent Hospital,
  Coronary Care Unit, 0599
Royal Infirmary, 0585, 0586
Royal Ottawa Hospital, 0098
Rural Health Center, Podad, 0283
Rutgers University, 1174
  Graduate School of Social Work, 1175
  School of Medicine, 1173

S.M.S. Medical College and Hospital, 0284, 0285
Sabbatsberg Hospital, 0462
Saga Medical School, 0388
Sahlgrenska Hospital, 0463, 0464
St. Bartholomew's Hospital, 0552
St. Elizabeth Hospital Medical Center, 0863
St. George's Hospital Medical School, 0553-0555
St. Joseph's Hospital and Medical Center,
  Barrow Neurological Institute, 0616
St. Luke's Hospital
  University College, 0296
St. Mary's Hospital, 1271
St. Paul's Hospital, 0101
St. Thomas's Hospital, 0556
St. Vincent's Hospital, 0297-0301
St. Vincent's Hospital,
  Smoker's Clinic, 0026, 0027
Sainte-Marguerite Hospital,
  Faculty of Medicine, 0248
Salo District Hospital, 0202
San Bernardino County Medical Center, 0650
San Francisco General Hospital, 0651
Santa Clara Valley Medical Center, 0652
Semmelweis University,
  Dental School, 0262
  Medical School, 0261
Servicio de Salud Metropolitano Oriente,
  Hospital del Salvador, 0140
Shanghai Cancer Institute, 0142, 0143
Shanghai First Medical College,
  School of Public Health, 0144, 0145
Shanghai Institute of Cardiovascular Diseases, 0146, 0147
Simon Fraser University, 0099, 0100
Smith Barney Harris Upham Co., Inc., 1270
Social Research Center, 0295
South Australian Health Commission,
  Health Promotion Services, 0024
South Australian Institute of Technology,
  Elton Mayo School of Management Studies, 0025
South Suburban Hospital, 0842
Southern Illinois University, 0844, 0845
  School of Law, 0843
Southwest Foundation for Biomedical Research, 1467

INDEX OF ORGANIZATIONS

- Stanford Cardiac Rehabilitation Program, 0654
- Stanford Research Institute International, 0653, 0655
- Stanford University, 0659, 0660
  - School of Medicine, 0656-0658, 0661
  - Stanford Heart Disease Prevention Program, 0662-0664
- State Department of Health Services,
  Resource for Cancer Epidemiology Section, 0665
- State Farm Insurance Co., 1448
- State of Washington, 1521
- State University of Limburg, 0398
- State University of New York, 1278-1281
- State University of New York, Buffalo, 1272-1276, 1282, 1283
- State University of New York, Stony Brook, 1277
- Studies on Smoking, 1397-1403
- Sully Hospital, 0600
- Swedish Farmers' Safety and Preventive Health Association, 0465
- Swedish National Food Administration, 0466
- Swiss Federal Institute of Technology,
  Institute of Behavioral Science, 0481-0487
- Swiss Institute for Experimental Cancer Research, 0488
- Sydney Hospital,
  Kanematsu Memorial Institute, 0028

- Tata Institute of Fundamental Research, 0286-0291
- Tel Aviv University,
  Sackler Faculty of Medicine, 0314, 0315
- Telemark Sentralsjukehus, 0413
- Temple University, 1404
  - School of Dentistry, 1405
  - School of Medicine, 1406
- Tennessee State University, 1449
- Texas College of Osteopathic Medicine, 1468
- Texas Technical University,
  Health Sciences Center, 1469
- Thought Technology Ltd., 0102
- Tianjin Medical College, 0148, 0149
- Tohoku University School of Medicine, 0389
- Trinity College, Dublin, 0302
- Trinity University, 1470
- Tufts-New England Medical Center, 1080
- Tulane University, 0965
  - School of Medicine, 0964, 0966

- U.E.R. Biomedicale des Sainte-Peres, 0249
- Ulleraker Hospital,
  Smoking Cessation Clinic, 0468
- Ullevaal Hospital, 0414
- Uniformed Services University of the Health Sciences, 1018-1021
- Unite de Recherches Pulmonaires, 0103
- Universidad de Cartagena, 0150
- Universitat Freiburg,
  Anatomisches Institut, 0184
- Universite Laval,
  Faculte de Medecine, 0104
- University College, Dublin, 0303
- University College Hospital, Ibadan, Nigeria, 0406
- University Hospital, Saskatoon, Saskatchewan, 0105
- University Hospital, Zurich, 0489
- University Hospital, Hamburg, 0185
- University Hospital of Aarhus,
  Institute of Cancer Research, 0154
- University Hospital of South Manchester, 0558, 0559
- University Hospital of Wales,
  University College of Medicine, 0601
- University Hospital, Rigshospitalet, 0165
- University Hospitals of Cleveland, 1355
- University Institute of Social and Preventive Medicine, 0490, 0491
- University Medical School, Krakow, Poland, 0438
- University of Aarhus, 0166, 0167
- University of Adelaide, 0029, 0030
- University of Alabama, 0609
- University of Alabama, Birmingham, 0605, 0606, 0608, 0610
  - School of Nursing, 0611
  - School of Public Health, 0607
- University of Alberta,
  Faculty of Medicine, 0106
- University of Amsterdam,
  Academisch Medisch Centrum, 0399
- University of Ankara, 0500
- University of Arizona,
  College of Medicine, 0617-0620
- University of Arkansas, 0625-0627
- University of Arkansas for Medical Sciences, 0624, 0628
- University of Athens, 0254, 0256
- University of Athens Medical School, 0253, 0255
- University of Bergen, 0170, 0415, 0416
  - Institute of Hygiene and Social Medicine, 0417
- University of Bern, 0492, 0493
- University of Bombay,
  Seth G.S. Medical College, 0292, 0293
- University of Bristol, 0560
- University of British Columbia, 0107, 0109, 0115, 0116
  - Pulmonary Research Laboratory, 0108
  - Vancouver General Hospital, 0110-0114
- University of California, 0672
- University of California, Los Angeles,
  Jonsson Comprehensive Cancer Center, 0666, 0667, 0689, 0690
- University of California, Berkeley,
  Institute of Human Development, 0674
  - Lawrence Hall of Science, 0675
  - School of Education, 0673
  - School of Public Health, 0676
- University of California, Davis, 0677
- University of California,
  Institute of Human Development, 0670
- University of California, Irvine, 0678
  - Medical Center, 0679
- University of California, Los Angeles, 0680, 0681, 0683, 0689, 0695, 0696
  - Center for Health Sciences, 0697
  - Harbor-UCLA Medical Center, 0692
  - School of Nursing, 0687
  - School of Public Health, 0684-0686, 0688, 0691
  - Schools of Medicine and Public Health, 0682
- University of California Medical Center, 0668
- University of California, San Diego, 0698, 0699, 0700
  - School of Medicine, 0671, 0701
- University of California, San Francisco, 0703, 0706, 0708-0710, 0712, 0714
  - Center for Social and Behavioral Sciences, 0707
  - Institute of Health Policy Studies, 0713
  - Langley Porter Neuropsychiatric Institute, 0704, 0705

INDEX OF ORGANIZATIONS

  Northern California Cancer Program, 0711
  School of Dentistry, 0702, 0715
University of California, Santa Cruz, 0716
University of Cambridge,
 Addenbrooke's Hospital, 0561
University of Cape Town Medical School, 0447
University of Chicago, 0847-0849
  Zoller Dental Clinic, 0846
University of Chile,
 Hospital del Salvador, 0141
University of Cincinnati, 1361
  College of Medicine, 1356-1360
University of Colorado, 0759
  Health Sciences Center, 0755, 0761, 0762
  Institute for Behavioral Genetics, 0754, 0757
  School of Dentistry, 0756
  School of Medicine, 0758
  School of Pharmacy, 0760, 0763
University of Copenhagen, 0169-0172
  Glostrup Hospital, 0168
University of Exeter,
 Washington Singer Laboratories, 0562, 0563
University of Florida, 0793-0795
  College of Medicine, 0796
University of Genoa,
 Institute of Hygiene, 0337-0339
University of Georgia, 0823, 0825
University of Georgia, Athens, 0825
  Coastal Plain Experiment Station, 0824
  Savannah River Ecology Laboratory, 1443
University of Ghent, 0057-0059
University of Glasgow, 0589
  Ruchill Hospital, 0588
University of Gothenburg, 0471-0475
University of Hawaii, 0829
University of Hawaii, Manoa,
 Cancer Center of Hawaii, 0830-0833
University of Heidelberg, 0188
  Clinical Faculty Mannheim, 0189
  Institute of Pathology, 0186, 0187
University of Helsinki, 0203
University of Hong Kong, 0258, 0259
University of Illinois, 0852, 0855
University of Illinois, Chicago, 0850
University of Illinois, Urbana-Champaign, 0851
University of Illinois,
 College of Medicine, 0853, 0854
University of Iowa, 0869, 0870
  College of Dentistry, 0875
  Toxicology Center, 0871, 0872
  University Hospitals and Clinics, 0873, 0874
University of Jyvaskyla, 0416
University of Kansas,
 College of Health Sciences, 0878, 0879
  Medical Center, 0877
University of Kentucky, 0889, 0891-0893, 0895, 0896, 0898, 0904, 0906-0908, 0911, 0912, 0916, 0917, 0920-0931, 0933
  Appalachian Fruit Research Laboratory, 0932
  School of Medicine, 0887, 0888, 0910, 0914, 0915, 0934
  School of Pharmacy, 0899, 0902, 0918, 0919
  Tobacco and Health Research Institute, 0890, 0894, 0900, 0903, 0905, 0909, 0913
University of Kentucky Medical Center, 0886, 0897, 0901
University of Kuopio, 0204, 0205
University of Leeds, 0564
University of Leiden, 0400
University of Limburg, 0401
University of London,
 Institute of Psychiatry, 0566, 0567
  School of Hygiene and Tropical Medicine 0565
University of Louisville, 0936
  School of Medicine, 0935, 0937-0942
University of Lowell, 1082
University of Lund,
 School of Dentistry, 0476
University of Mainz, 0190
  Institute for Physiological Chemistry, 0174
University of Manitoba, 0117-0119
University of Maryland, 1025, 1028, 1030, 1032
  School of Dentistry, 1029
  School of Medicine, 1022-1024, 1026, 1027, 1031
University of Massachusetts Medical School, 1083-1093
University of Medicine and Dentistry of New Jersey,
 New Jersey Medical School, 1176
University of Melbourne, 0031, 0035
  Repatriation General Hospital, 0032-0034, 0036
University of Miami,
 Spanish Family Guidance Center, 0797
University of Michigan, 1103, 1107
  Institute for Social Research, 1104
  School of Public Health, 1105, 1106
University of Milan, 0331, 0332
  Institute of Occupational Health, 0340
University of Minnesota, 1118-1120, 1122, 1123, 1127-1134, 1136, 1137
  College of Biological Sciences, 1117
  School of Nursing, 1124
  School of Public Health, 1121, 1135
  Smoking Research Laboratory, 1125
University of Missouri, Columbia, 1144, 1145
University of Missouri,
 Health Science Center, 1143
University of Nebraska, Lincoln,
 Nebraska Prevention Center for Alcohol and Drug Abuse, 1161
University of Nebraska,
 Medical Center, 1154-1160
University of Nevada, Reno, 1162
University of New Mexico, 1189-1191
University of New South Wales, 0017
University of New South Wales,
 School of Community Medicine, 0037, 0038
University of Newcastle, 0039
  Faculty of Medicine, 0040
University of Nijmegen, 0402
University of North Carolina, 1322-1324
  Moses H. Cone Memorial Hospital, 1325
  School of Medicine, 1327
  School of Nursing, 1326
University of Nottingham,
 University Hospital and Medical School, 0568, 0569
University of Occupational and Environmental Health, 0390
University of Oklahoma, 1365
  Health Sciences Center, 1363, 1364
University of Oregon, 1376-1380
  School of Medicine, 1375

INDEX OF ORGANIZATIONS

- University of Oslo,
  - Institute of Social Medicine, 0418, 0419
- University of Otago,
  - Medical School, 0405
- University of Ottawa, 0120
  - School of Medicine, 0121
  - School of Nursing, 0122
- University of Oulu, 0206-0212, 0215, 0216
- University of Oxford, 0573
  - Radcliffe Infirmary, 0570-0572
- University of Pennsylvania, 1411, 1412, 1415
  - Johnson Foundation, 1409
  - School of Medicine, 1413, 1414
  - The Wharton School, 1410
- University of Pennsylvania Hospital, 1408
- University of Perugia,
  - Hygiene and Preventive Medicine Institute, 0341-0343
- University of Pittsburgh, 1417, 1419, 1420-1422, 1424, 1425
  - School of Public Health, 1416, 1418, 1423
- University of Queensland, 0041
- University of Reading, 0574
- University of Rhode Island, 1434, 1435
- University of Rochester, 1289
  - Center for Brain Research, 1284-1286
  - School of Medicine, 1287, 1288
- University of San Francisco,
  - Institute of Chemical Biology, 0717
- University of Sheffield, 0575
- University of South Alabama,
  - College of Medicine, 0612, 0613
- University of South Florida, 0798, 0799
- University of Southampton, 0576, 0578
  - Southampton General Hospital, 0577
- University of Southern California, 0718
  - Health Behavior Research Institute, 0724-0729
  - School of Medicine, 0719-0723, 0730-0733
- University of Stockholm, 0477
- University of Sussex,
  - Developmental Psychology Group, 0579
- University of Sydney, 0043, 0044
  - Commonwealth Institute of Health, 0009
  - Westmead Hospital, 0042
- University of Tampere,
  - Institute of Clinical Sciences, 0213
- University of Tasmania,
  - Queen Alexandra Hospital, 0045
- University of Tennessee,
  - College of Medicine, 1450
- University of Texas,
  - Health Science Center at Houston, 1472-1474, 1480, 1481, 1483
  - Health Science Center of San Antonio, 1475, 1479
  - School of Allied Health Sciences, 1477, 1482
  - School of Public Health, 1478
- University of Texas Medical Branch, Galveston,
  - Cancer Center, 1476
- University of the West Indies,
  - Queen Elizabeth Hospital, 0053
- University of Torino, 0344-0346
  - Chair of Cancer Epidemiology, 0347
- University of Toronto, 0123, 0124
  - Gage Research Institute, 0126
  - Mount Sinai Hospital, 0125
  - School of Physical and Health Education, 0126
- University of Tromso,
  - Institute of Community Medicine, 0420
- University of Trondheim, 0421, 0422
- University of Turku, 0214
- University of Utah,
  - Graduate School of Social Work, 1493
  - School of Medicine, 1489-1492
- University of Vermont, 1498, 1500-1504
- University of Vermont,
  - School of Medicine, 1497, 1499
    - Institute of Hygiene, 0050
- University of Wales,
  - College of Medicine, 0602
- University of Washington, 1523, 1525-1529
  - Child Development and Mental Retardation Center, 1533
  - College of Education, 1524
  - School of Medicine, 1522
  - School of Public Health and Community Medicine, 1530, 1531
  - School of Social Work, 1532
- University of Waterloo, 0127
  - Faculty of Human Kinetics and Leisure Studies, 0129
  - Faculty of Mathematics, 0128
- University of Western Australia, 0046
  - Busselton Health Centre, 0008
  - Royal Perth Hospital, 0047
- University of Western Ontario, 0130-0138
- University of Wisconsin, 1552-1554
  - School of Veterinary Medicine, 1555
  - Wisconsin Survey Research Laboratory, 1551
- University of Wyoming, 1560-1562
- University of Wyoming, Laramie, 1559
- University of Zurich,
  - Institute of Pathology, 0495
  - Psychiatric Clinic, 0494
- U.S. Department of Agriculture, 1494
  - Science and Education Administration,
    - Agricultural Research Service, 0603, 0804-0806, 0821, 0822, 0881-0884, 1304, 1328, 1329
      - Beltsville Agricultural Research Center, 1033, 1034
      - Clemson University, 1444
      - Cornell University, 1291
      - Georgia Coastal Plain Experimental Station, 0826
      - North Carolina State University, 1330
      - Plum Island Animal Disease Center, 1292
      - Tobacco Research Laboratory, 1331
      - University of Kentucky, 0943-0953
      - University of Maryland, 1035
      - University of Tennessee, 1451
      - University of Wisconsin, 1556
      - Virginia Polytechnic Institute, 1510
    - Economic Research Service, 0784
    - Oxford Tobacco Research Laboratory, 1321
- U.S. Department of Health and Human Services,
  - Office on Smoking and Health, 0972-0974
  - Public Health Service,
    - Alcohol, Drug Abuse, and Mental Health Administration,
      - National Institute on Drug Abuse, 0971, 1012-1014
      - National Institute of Mental Health, 0983
    - Centers for Disease Control, 0808-0816
      - National Institute for Occupational Safety and Health, 1350, 1543-1545
    - National Institutes of Health,

INDEX OF ORGANIZATIONS

    National Cancer Institute, 0215, 0216, 0639, 0982, 0984-0986, 0988-0990, 0993, 1009-1011
    National Heart, Lung, and Blood Institute, 0987
    National Institute of Environmental Health Sciences, 1313-1316
U.S. Environmental Protection Agency, 0783
U.S. Veterans Administration, 0629, 0633, 0742-0746, 0769, 0827, 0857, 0858, 0955, 0970, 1096, 1097, 1149, 1185, 1186, 1299-1302, 1428, 1437-1441, 1488, 1506, 1546
U.S. Veterans Administration Hospital, 0622, 1237
U.S. Veterans Administration Medical and Regional Office Center, 1505
U.S. Veterans Administration Medical Center, 0614, 0621, 0623, 0630-0632, 0693, 0694, 0735, 0738-0741, 0748, 0764, 0768, 0785, 0800-0803, 0834, 0856, 0954, 0967, 0968, 1036, 1095, 1108-1110, 1138, 1139, 1146-1148, 1165, 1177-1184, 1294-1298, 1332-1337, 1381, 1426, 1427, 1436, 1459, 1486, 1487, 1496, 1534-1538, 1557, 1558
    Baylor College of Medicine, 1484, 1485
    Brentwood Division, 0736
    Enzymology Research Laboratory, 0734
    Mount Sinai School of Medicine, 1293
    School of Medicine, 0767
    West Los Angeles, 0737
U.S. Veterans Administration Outpatient Clinic, 0747, 1094
Utah Department of Health,
    Bureau of Health Promotion/Risk Reduction, 1495

Vanderbilt Medical Center, 1452
Vanderbilt University, 1454-1456
    Health Care Research Project, 1457
    School of Medicine, 1453, 1458
Verband Deutscher Rentenversicherungstrager, 0191
Vestfold Central Hospital, 0423
Virginia Commonwealth University, 1512-1514
Virginia Commonwealth University,
    Medical College of Virginia, 1511

Washburn University, 0880
Washington Department of Social and Health Services/Epidemiology, 1539
Washington State Health Laboratories - Epidemiology, 1540
Washington State University, 1542
    Social Research Center, 1541
Washington University, 1150, 1151
Wayne State University, 1112, 1113
    School of Medicine, 1111
Wesley Hospital,
    Queensland Fertility Group Laboratory, 0048
West of Scotland Cancer Surveillance Unit, 0590-0591
Western General Hospital,
    Infertility Clinic, 0592
Western Institute of Behavioral Research, 0749
Western Kentucky University, 0957
Westmead Hospital, 0031
Wingate Institute, 0316
Worcester Foundation for Experimental Biology, 1098
World Health Organization,
    WHO Smoking and Health Programme, 0496

Yale University, 0774
    New Haven Medical Center, 0773
    School of Medicine, 0772
    School of Nursing, 0771
Yeshiva University,
    Albert Einstein College of Medicine, 1303
Yokohama City University,
    School of Medicine, 0391

BEST [illegible]

BLANK PAGE

INDEX OF SPONSORS

AB Leo Foundation, 0027, 0468, 0520, 0554
Academy of Finland, 0196, 0200
Academy of Science and Literature, Federal Republic of Germany, 0174
Addiction Research Foundation, Canada, 0061
Agriculture Canada, 0062
Aichi Cancer Center Research Institute, 0349-0352
Aichi University of Education, 0353
Alberta Inter-Agency Council on Smoking and Health, Calgary, 0063
Alexander von Humboldt Foundation, Federal Republic of Germany, 0141
All Union Cardiological Research Center, USSR, 0501
Allegheny County Health Department, 1382, 1383
Allegheny County Mental Health, Mental Retardation, and Drug and Alcohol Program, 1421
Allmanna BB s Minnesfond, Sweden, 0449
Amberley Associates, 1342
American and Colorado Health Associations, 0755
American Cancer Society, 0666, 0684, 0687, 0675, 0688, 0690, 0693, 0707, 0720, 0731, 0732, 0756, 0771, 0773, 1193, 1194, 1269, 1341, 1353, 1527
American Health Foundation, 1278, 1279
American Heart Association, 0623, 0934, 0942, 1074, 1171, 1352, 1366, 1412, 1452, 1458, 1512, 1554
American Institute for Preventive Medicine, 1101
American Lung Association, 0493, 0604, 0624, 0669, 0722, 0726, 0835, 1031, 1124, 1150, 1218, 1219, 1289, 1352, 1364, 1452, 1524
American Lung Association of California, 0716
American Lung Association of Florida, 0793
American Lung Association of Maryland, 1015
American Lung Association of Western New York Inc., 1283
American Tobacco Manufacturers Research Fund, 0530
Anti-Cancer Council of Victoria, 0005
Arizona Lung Association, 0620
Arnold Yeldham and Mary Raine Research Foundation, 0008
Association Suisse des Fabricants de Cigarettes, 0488
Associazione Italiana per la Ricerca sul Cancro, 0317
Asthma Foundation of Victoria, Australia, 0023
Atomic Energy Control Board of Canada, 0097
Australian Government, 0004, 0007
Australian Institute of Petroleum Ltd., 0035
Australian Tobacco Research Foundation, 0028, 0031, 0042-0044

Bangladesh Association for Cancer Services, 0051, 0052
Baystate Medical Center, 1037
Behringwerke, 0547
Belgian Cooperation Service, 0055
Belgium Ministry of Public Health, 0059
Belgium National Fund for Scientific Research, 0059
Ben-Gurion University of the Negev, 0304
Beth Israel Hospital, 1166
Biomedical Research Support Grant, 1122
BIOSPEC, Inc., 1429
Bland-Sutton Institute of Pathology, 0536, 0537
Blue Cross of Northwest Ohio, 1341
Bombay Municipal Corporation, 0293
Bowling Green State University, 1343
British American Tobacco Co., 0506
British Broadcasting Corporation, 0507
British Columbia Health Care Research Foundation, 0107, 0111-0114
British Columbia Lung Association, 0076, 0101, 0108, 0110-0114
British Education Council, 0570
British Heart Foundation, 0548, 0570
British Tobacco Industry, 0535
Brown University, Miriam Hospital, 1431, 1432

Cabot Family Charitable Trust, 1068
California Maternal Child Health, 0692
California Research and Medical Education Fund, 0716
California State Air Resources Board, 0682
Cambridge Quest Foundation, 0762
Canada, Department of National Health and Welfare, 0066-0073, 0080, 0090, 0121, 0123, 0126, 0127
Canadian Cancer Society, 0123
Canadian Health Promotion Contribution Program, 0069
Canadian Heart Foundation, 0069
Canadian Medical Research Council, 0101, 0108, 0111-0115, 0125
Canadian Tobacco Council, 0229, 0230
Cancer Association of New Orleans, 0964
Cancer Foundation of Western Australia, 0006
Cancer Research Campaign, United Kingdom, 0505, 0518, 0525, 0531, 0532, 0552, 0576, 0589, 0594
Cancer Research Institute, India, 0266
Cancer Society of New Zealand, 0403
Cardiff Royal Infirmary, 0595
Carle Clinic Association Wellness Center, 0836
Carmel Hospital, Israel, 0306, 0307
Carnegie Corporation, 1069
Carter Center, Emory University, 0810, 0814
Carter County Government, 1445
Center for Health Research, 1368
Center for Industry and Health Care, 1047
Center for Ulcer Research and Education, 0650
Central Government of Upper Austria, Department of Health, 0049
Central Medical Board Finland, 0209
Central Tobacco Research Institute, India, 0267, 0268
Centro de Investigaciones Toxicologicas, Argentina, 0001
Centro Nazionale Ricerche, Italy, 0346, 0347
Charles Camsell General Hospital, 0075
Chemie-Linz-AG, 0049
Chest, Heart and Stroke Association, United Kingdom, 0514, 0600
Chiba University, Japan, 0358
City of Hope National Medical Center, 0636, 0637
City of Oslo, 0414
Colorado Medical Services Foundation, 0758
Colorado State University, 0750, 0751
Colt Foundation, 0509
Commission of European Communities, 0221, 0294
Committee on Smoking and Health, Federal Republic of Germany, 0183
Commonwealth Department of Health, Australia, 0009, 0016, 0021, 0079

References following all entries are to Description Numbers.

INDEX OF SPONSORS

Community Health Projects, Inc., 0638
Conrad N. Hilton Foundation, 1069
Consiglio Nazionale Delle Ricerche, Progetto Finalizzato Oncologia, 0317, 0320
Copernicus Academy of Medicine, Poland, 0426-0428
Cotton Incorporated, 1309
Council for Tobacco Research, U.S.A., Inc., 0190, 0203, 0452, 0454, 0566, 0609, 0612, 0616, 0671, 0762, 0763, 1005, 1007, 1050, 1064, 1082, 1111, 1230, 1239, 1240, 1250-1252, 1259, 1284, 1285, 1287, 1352, 1354, 1410, 1433, 1455, 1456, 1479, 1555
Council of Scientific and Industrial Research, India, 0264
Creighton University School of Medicine, 1152
Cystic Fibrosis Foundation, 0870
Czechoslovakian State Government, 0155

D.M.S.S., United Kingdom, 0556
Daicel Chemical Industries Ltd., Japan, 0359
Dalhousie University, Canada, 0077
Danish Cancer Society, Laboratory of Environmental Carcinogenesis, 0164
Danish Medical Research Council, 0164, 0168
Danish Sports Research Council, 0169
Danish Working Environment Fund, 0167
Darlington Memorial Hospital, England, 0511
Defense Institute of Physiology and Allied Sciences, 0292
Del laegevidenskabelige Forskningsrad, 0161
Delegation Generale a la Recherche Scientifique et Technique, 0232, 0233, 0235
Departement de Sante Communautaire, Gaspe, Canada, 0084
Derer's Hospital, Czechoslovakia, 0152
Deutsches Krebsforschungszentrum, Federal Republic of Germany, 0175
District Institute cf National Health, Czechoslovakia, 0153
Dow Chemical Corporation, 0659, 1099
Duetsche Forschungsgemeinschaft, 0180
Dundee University, 0580
Dutch Cancer Foundation, 0398
Dutch Foundation for Preventive Research, 0397
Dutch Heart Foundation, 0397
Dutch Ministry of Social Affairs, 0402
Dutch Municipal Health Department, 0397

E.I. du Pont de Nemours and Co., 0786, 1443
East Carolina University School of Medicine, 1311
East Tennessee State University, 1446
Ecole Nationale Superieure de Chimie, 0217
Economic and Social Research Institute, Dublin, 0294
Education Ministry of Japan, 0365
Egyptian Government, 0581
Electric Power and Research Institute, 1063
Environmental Agency, Japan, 0386
Environmental Pollution Control Center, 0361, 0362
EPRI, 0618
European Economic Community, 0252

Faculte de Med Pitie-Salpetriere, 0218
Family Health International, 0811
Family Heart Study, 1369
Federal Trade Commission, 0777
Feeling Fine Production Co., 0724, 0725
Finnish Academy, 0204
Finnish Cancer Research Foundation, 0212
Finnish Council for Exercise Sciences, 0204
Finnish Government, 0197
Finnish Medical Board, 0204
Finnish Medical Research Council, 0203
First of May Flower Annual Campaign for Children's Health, 0449
Fond National de la Recherche Scientific Medical, 0056
Fonds voor Wetenschappelijk Geneeskundig Onderzoek, Belgium, 0054
Forschungsgesellschaft Rauchen und Gesundheit, Federal Republic of Germany, 0483
Foundation of the Sick, the Netherlands, 0401
Fox Chase Cancer Center, 1386
French Department of Health, 0238
Fujita-Gakuen Health University, Japan, 0363
Fukuoka-ken Anti-cancer Society, 0390

G.S.F. Munchen, Federal Republic of Germany, 0312
G.S.F. Research Center, Neuherberg, Federal Republic of Germany, 0176, 0177
General Clinical Research Center, 1224
General Hospital of Monfalcone, 0318
Gentofte Hospital, 0160
Georgetown University School of Medicine, 0778
Georgia Agricultural Commodity Commission for Tobacco, 0823, 0824
Glaxo Australia, 0027
Glaxo Group Research, England, 0580
Glaxo Pharmaceutical Co., 0037
Glostrup Hospital, 0168
Greek Cancer Society, 0255, 0256
Greek Ministry of Health, 0255, 0256
Greek Ministry of Social Services, 0254
Group Health Associates, 1351
Gujarat Cancer and Research Institute, India, 0272
Gujarat State Government India, 0269, 0271

Harvard School of Public Health, 1060
Haut Comite d'Etude et d'Information sur l'Alcoolisme, 0231, 0237
Health and Safety Executive, 0515
Health Campaign Fund, China, 0148
Health Commission of Victoria, 0011
Health Department of Greece, 0251
Health Department of Western Australia, 0012, 0013, 0014, 0015
Health Education Bureau, Ireland, 0295
Health Education Council, United Kingdom, 0507, 0523, 0526, 0548, 0553, 0562, 0565, 0568, 0569, 0572, 0593, 0596, 0597
Health Effects Institute, Cambridge, Massachusetts, 0649, 0677, 1003, 1469
Health Improvement Systems, 1085
Health Promotion Directorate, Manitoba, 0081, 0082, 0083
Heartbeat Wales, 0596, 0597
Helsinki University Central Hospital, 0192
Hoffmann-La Roche, 1043
Hokkaido Prefecture, Japan, 0366
Hong Kong Anti-Cancer Society, 0258
Hospital del Salvador, 0140

INDEX OF SPONSORS

Hospital for Sick Children Foundation, Canada, 0077
Hospital of Monfalcone, Italy, 0348
Huddinge University Hospital, 0452

I N I C Portugal, 0439, 0440
Imperial Tobacco Co Ltd , 0561
Independent Scientific Committee on Smoking and Health, 0533
Indian Council of Agricultural Research, 0267, 0268
Indian Council of Medical Research, 0265, 0274, 0282, 0293 GFG
  Indian Government, 0269, 0271, 0273
Indiana State Board of Health, 0859
Indiana University, 0859
Institut d'Etudes et Recherches Pneumophtisiologiques, 0241, 0248
Institut de Protection et de Surete Nucleaire, 0242
Institut de Recherche en Sante et en Securite du Travail du Quebec, 0087
Institut National de la Sante et de la Recherche Medicale, 0219, 0222-0224, 0226, 0227, 0229, 0230, 0232-0239, 0241, 0248, 0497
Institut National de Recherche et de Securite, France, 0243, 0244
Institut Territorial de Recherches Medicales Louis Malarde, Tahiti, 0497
Institute for Clinical and Experimental Medicine, Czechoslovakia, 0154
Institute of Child Health, Greece, 0251
Institute of Community Health, 0161
Institute of Hygiene and Public Health, Romania, 0444
Institute of Preventive Cardiology, Union of Soviet Socialist Republics, 0502, 0503
Instituto Mallattie Respiratorie Dell' Universita, Milano, 0323
Instituto Nazionale per la Ricerca Sul Cancro, 0325
International Agency for Research on Cancer, 0245, 0250
International Lead Zinc Research Organisation, 0529, 1344
Iowa Lutheran Hospital, 0865
Irish Heart Foundation, 0297, 0303
Israel Cancer Association, 0310, 0311
Israeli Cancer Society, 0304, 0307
Istituto Nazionale per la Ricerca sul Cancro, 0324
Istituto Nazionale per lo Studio e la Cura dei Tumori, 0326
Italian Association for Cancer Research, Milan, 0331, 0332
Italian League Against Cancer, Milan, 0331, 0342
Italian Ministry of Education, 0345
Italian Ministry of Health, 0342
Italian National Research Council, 0321, 0331, 0332, 0337, 0339, 0343

Japan Institute of Public Health, 0368-0372
Japan Ministry of Education, Science and Culture, 0257, 0352, 0355, 0380, 0381, 0388
Japan Ministry of Health and Welfare, 0384
Japan Ministry of Labor, 0382
Japan Tobacco and Salt Public Corporation, 0349, 0354, 0356, 0357, 0367-0369, 0371-0373, 0376-0380, 0387, 0389
Johns Hopkins University, 1000, 1004
Johnson County Lung Association, 0870
JRB Associates, Virginia, 1518
Juho Vainio Foundation, Finland, 0206-0208, 0210

KABC Television, 0724, 0725
Kaiser Foundation Research Institute, 0642
Kaiser-Permanente Medical Care Program, 0643, 0644
Kansas City, Missouri Health Department, 1141
Kansas Department of Health and Environment, 0876
Karolinska Institute, Sweden, 0455, 0456
Kean College of New Jersey, 1168, 1169
Kellogg Foundation, 0074
Kentucky Department of Human Resources, 0957
Kentucky Tobacco and Health Research Institute, 0886-0889, 0892, 0894-0897, 0900-0902, 0904-0908, 0910, 0912-0917, 0935, 0937, 0939, 0941, 0983, 1325, 1446
Kentucky Tobacco Research Board 0886, 0890, 0903, 0918, 0919
Khyber Medical College, Peshawar, Pakistan, 0425
King Edward VII Memorial Fund, 0590
Kingston Polytechnic, England, 0524, 0525
Korea Ginseng and Tobacco Research Institute (K85TP-031), 0441, 0443

L Sacco Hospital, Milan, Italy, 0328, 0329
Laboratoire d'Allergologie, 0247
Laboratorio Fleury, Brazil, 0060
Lady Davis Fellowship, Jerusalem, 1282
Lahey Clinic Medical Center, 1071, 1072
Lega Italiana per la Lotta Contro i Tumori, 0330
Leukaemia Research Fund, England, 0510
Lewis and Clark College, 1368
Loma Linda University, 0645
Louis and Rose Klock Foundation, 1259

MacArthur Foundation, 0670, 0688, 0694, 0775, 1393, 1394
Mahidol University, Thailand, 0498
Manitoba Medical Services Foundation, 0118, 0119
March of Dimes Birth Defects Foundation, 0755, 0758, 1344
Margaret E Early Medical Research Trust, 0730
Marion Gardner Jackson Trust, 1073
Marshfield Clinic, 1548
Massachusetts Department of Public Health, 0713
Maxicare Research and Education Foundation, 0646
McArthur Foundation, 0688
Mead Johnson and Co., 0878
Medical College of Oita, 0381, 0382
Medical College of Wisconsin, 1549
Medical Control Centers Inc., 1170
Merrell-Dow Pharmaceuticals Inc., 0137, 0681, 1043, 1079, 1348, 1355
Metropolitan Life Insurance Co., 1243
Michigan Hospital Association Mutual Insurance Co., 1391
Michigan Molecular Institute, 1102
Middlesex Hospital, England, 0538
Ministry for Research and Technology, Federal Republic of Germany, 0176
Ministry of Public Health, Peoples Republic of China, 0144, 0145
Ministry of Social Affairs of Quebec, 0090
Minnesota Medical Foundation, 1119
Mitsubishi Acetate Co Ltd , 0383
Moody Foundation, 1482

Nassau Hospital, 1249
Nationaal Fonds voor Wetenschappelijk Onderzoek, 0056

INDEX OF SPONSORS

National Academy of Science, 1397
National Academy of Sciences, Jerusalem, 0308
National Board of Electricity, Italy, 0333
National Board of Health, Finland, 0194, 0195, 0199, 0200, 0201, 0205
National Cancer Association of South Africa, 0445
National Cancer Center Research Institute, Japan, 0385
National Cancer Institute of Canada, 0065, 0091-0093, 0123
National Center for Atmospheric Research, 0752
National Committee Against Respiratory Diseases and Tuberculosis, France, 0240
National Council for Research and Development, Israel, 0312
National Council for Research, Argentina, 0001
National Council on Smoking and Health, Norway, 0407, 0408, 0409, 0410
National Health and Medical Research Council of Australia, 0008, 0022, 0040
National Health Research and Development Program, Canada, 0077
National Health Research Scholar Award, 0130, 0132, 0133
National Health Service England, 0585
National Heart Foundation of Australia, 0008, 0016, 0038
National Heart Foundation of New Zealand, 0404, 0405
National Institute on Cancer Research, Italy, 0334, 0335, 0336
National Public Health Institute, Finland, 0197, 0198
National Research Council of Canada, 0064
National Science Foundation, 0752, 1047
National Scientific and Technical Committee, Peoples Republic of China, 0143
National University of Singapore, 0392
NATO, 0651
Nebraska State Department of Health, 1153, 1158, 1161
Netherlands Cancer Foundation, 0396
Netherlands Ministry of Health and Environmental Hygiene, 0397
New Jersey State Department of Higher Education, 1168, 1169
New Mexico Institute of Mining and Technology, 1188
New South Wales State Cancer Council, 0040
New York State Department of Health, 1254, 1255
New York State Health Research Council, 1266
New York University Medical Center, 1259
New Zealand Medical Research Council, 0405
Neye Foundation, 0157
North Carolina Lung Association, 1309
North Carolina State University, 1319
North Dakota State Department of Health, 1338
North Dakota State University, 1340
North East Thames Region Award, 0528
Northeast Foundation, Exeter, 0545
Northern California Cancer Program, 0711
Northwest Ohio Heart Association, 1341
Northwest Ohio Lung Association, 1341
Northwest Thames Regional Health Authority, 0546
Northwestern University, 0840
Norwegian Cancer Society, 0412, 0417
Norwegian Council for Scientific and Industrial Research, 0422
Norwegian Council on Cardiovascular Disease, 0420
Norwegian Government, 0411
Norwegian Radium Hospital, 0412
Norwegian Research Council for Science and the Humanities, 0420
Norwegian Society for Fighting Cancer, 0417
Notre Dame Foundation, 0094
Nova Scotia Department of Health, 0077
Nuffield Dominions Trust and Lundbeck Ltd., 0571

Office of Monopoly, Republic of Korea, 0442
Ohio Dental Association, 1348
Oklahoma State Department of Health, 1362
Ontario Cancer Treatment and Research Foundation, 0124
Ontario Heart Foundation, 0127
Ontario Ministry of Agriculture and Food, 0062
Ontario Ministry of Health, 0127, 0138
Ontario Ministry of Labour, 0096, 0097
ntario Thoracic Society, 0130, 0136
regon Lung Association, 1381
tergotlands Lans Landsting, Sweden, 0457
Oxford District Research Committee, 0571

Paulo Foundation, 0202
Pennsylvania Department of Health, 1395
Pennsylvania Hospital Insurance Co., 1391
Pennsylvania Medical Society Insurance Co., 1391
Pharmacon Research Foundation, Inc., 0936
Pneumoconioses Research Institute, 0182
Polish Academy of Sciences, 0429, 0430
Polish Government, 0432
Postgraduate Institute of Medical Education and Research, India, 0275-0282
Preventie Fonds, 0399
Prevention Research Center, 1396
Prince Georges County Public Schools, 1015
Prince Henry Hospital, 0017
Process and Instruments Corp., 1263, 1264
Provincial Blood Donation Centre, Poland, 0436, 0437
Pulmonary Associates, 0615

Quebec Lung Association, 0088
Queensland Fertility Group Laboratory, 0048

R.J. Reynolds, Inc., 0824, 1030
Regional Health Authority, United Kingdom, 0344
Regione Lombardia, Italy, 0322
Regione Piemonte, 0317
Research Institute of Applied Electricity, 0364
Research Institute on Alcoholism, 1266
Reynolds Tobacco Research, 0567
Rigshospitalet, Denmark, 0165
Robert Wood Johnson Foundation, 0605, 0697, 1242, 1324
Romanian Minstry of Chemical Industry, 0444
Royal Children's Hospital, Melbourne, 0023
Royal Free Hospital, England, 0550, 0551
Royal Infirmary, Glasgow, 0586
Royal Perth Hospital Research Fund, 0008
Rutgers University, 1173, 1174

Sahlgrenska Hospital, Gothenburg, 0464
St. Luke's Hospital, Ireland, 0296
St. Luke's Hospital, Milwaukee, Wisconsin, 1547
Salo District Hospital, 0202
Sands House Association, 0756
Sapir Foundation, 0307

INDEX OF SPONSORS

Saskatchewan Lung Association, 0105
Scottish Health Education Group, Health Education Council, 0588
Scottish Home and Health Department, 0582, 0584, 0590
Scripps Foundation, 0652
Secretariat d' Etat Charge de la Sante, Paris, 0478
Securite Sociale, France, 0241, 0248
Semmelweis University Medical School, 0261, 0262
Servicio de Salud Metropolitano Oriente, 0140
Shanghai Institute of Cardiovascular Diseases, 0146, 0147
Smith Barney Harris Upham Co., Inc., 1270
Smith Kline and French Laboratories, 0650
Smokeless Tobacco Research Council Inc., 0819, 0841, 0875, 1029, 1058, 1059, 1093, 1357, 1358, 1489, 1500, 1507
Social Sciences and Humanities Research Council of Canada, 0085
Societe d'Etude de al Dependance Tabagique, 0249
South African Medical Research Council, 0445, 0446
South Australian Health Commission, 0024, 0029, 0030
South Australian Institute of Technology, Elton Mayo School of Management Studies, 0025
South Suburban Hospital, Illinois, 0842
Southampton University, 0577
Southern Illinois University, 0844
State Farm Insurance Companies, 1448
State Government of Victoria, 0005
State's Alcohol Monopoly Co., Finland, 0200
State Smoking and Health Project, Western Australia, 0018
Sudan Anti-Smoking Society and Ahfad College for Women, 0448
Swedish Cancer Society, 0459, 0462
Swedish Farmers' Safety and Preventive Health Association, 0465
Swedish Government, 0471
Swedish Governmental Committee on Radon in Homes, 0453
Swedish International Development Agency, 0496
Swedish Medical Research Council, 0452, 0458, 0461, 0464, 0472
Swedish National Bank Tercentenary Fund, 0473, 0474
Swedish National Food Administration, 0466
Swedish Tobacco Co., 0450, 0451, 0458, 0462, 0463, 0469, 0476, 0477
Swedish Work Environment Fund, 0460
Swiss Association Against Tuberculosis and Lung Diseases, 0493
Swiss Association of Cigarette Manufacturers, 0481, 0482, 0484, 0486, 0489
Swiss Hospital Association (VESKA), 0492
Swiss National Science Foundation, 0492, 0494

Tata Institute of Fundamental Research, 0287, 0289, 0290
Tel Aviv University, 0308, 0314, 0315
Telemark Sentralsjukehus, Norway, 0413
Temple University, 1405
Tenneco Inc., J S. Abercrombie Foundation, 1486
Texas College of Osteopathic Medicine, 1468
Texas Planning Council on Developmental Disabilities, 1464
Thought Technology Ltd., 0102
Tianjin Medical College, China, 0149
Tobacco Advisory Council, United Kingdom, 0514, 0519
Tobacco Companies Consortium, 0555
Tobacco Industry Panel, 0181
Tobacco Institute, 1318
Tobacco Products Research Trust, 0533
Tochigi Prefecture Government, 0360
Tokyo Medical College, 0462
Town Council of Milan, Italy, 0323
Tulane University, 0964

Turkish Scientific and Technical Research Council, 0500

U.K. Department of Health and Social Security, 0517, 0527, 0541, 0556-0559, 0582
U.K. Medical Research Council, 0504, 0508, 0514, 0521, 0522, 0534, 0540-0543, 0549, 0560, 0565, 0573, 0574, 0587, 0590
U.K. Ministry of Defense, 0539
U.S. Agency for International Development, 0811
U.S. Department of Agriculture, 0603, 0604, 0776, 0784, 0804-0806, 0821, 0822, 0826, 0868, 0881-0885, 0891, 0898, 0911, 0920-0933, 0943-0953, 0978, 1030, 1032-1035, 1238, 1261, 1291, 1292, 1304, 1317, 1321, 1328-1331, 1444, 1451, 1494, 1510, 1556
U.S. Department of Defense, 1020, 1081, 1442, 1466
  Department of the Air Force, 1465, 1471
  Department of the Army, 1167, 1290
U.S. Department of Energy, 1187, 1189, 1443, 1515
U.S. Department of Health and Human Services,
  Public Health Service, 0095, 0291, 0640, 0761, 0859, 1226, 1287, 1484, 1485
    Alcohol, Drug Abuse, and Mental Health Administration, 0978, 1055
      National Institute on Alcohol Abuse and Alcoholism, 0648, 0796, 0816, 0976, 0979, 0980, 1023, 1046, 1262, 1265, 1266, 1293, 1509
      National Institute on Drug Abuse, 0647, 0670, 0674, 0683, 0703-0706, 0724, 0727, 0737, 0754 0757, 0779, 0799, 0817, 0847, 0850, 0975, 0991, 0992, 0995, 0996, 1012-1014, [illegible], 1049, 1056, 1057, 1103, 1104, 1107, 1118, 1125, 1126, 1131, 1132, 1134, 1136, 1222, 1225, 1232, 1233, 1245, 1246, 1248, 1286, 1320, 1367, 1372, 1373, 1393, 1394, 1493, 1511, 1529, 1541, 1550
      National Institute of Mental Health, 0673, 0686, 0837, 0976, 0983, 1080, 1308, 1406, 1462, 1477
    Centers for Disease Control, 0808, 0809, 0811, 0813, 0815, 0816, 0980, 1338
      National Institute for Occupational Safety and Health, 0635, 0656, 0665, 0980, 1061, 1247, 1350, 1361, 1543-1545
    Food and Drug Administration, 0978, 1009, 1010, 1039, 1043, 1052
    Health Resources and Services Administration, 0657, 0658
    National Center for Health Services Research, 0646, 1175
    National Institutes of Health, 0590, 0620, 0624, 0628, 0640, 0668, 0756, 0762, 0778, 0782, 0794, 0817, 0820, 0840, 0870, 0961, 0978, 0980, 0999, 1115, 1119, 1343, 1343, 1454, 1526, 1528
      National Cancer Institute, 0050, 0089, 0129, 0142, 0203, 0228, 0254, 0286, 0288, 0320, 0417, 0606, 0639, 0641, 0660-0662, 0667, 0684, 0685, 0708, 0712, 0714, 0715, 0721-0723, 0728, 0767, 0770, 0773, 0782, 0829, 0830, 0832, 0833, 0841, 0855, 0861, 0862, 0871, 0879, 0923, 0925-0927, 0938, 0960, 0982, 0984-0986, 0988-0990, 0993, 1000, 1001, 1006, 1009-1011, 1016-1018, 1027, 1046, 1060, 1065, 1067, 1070, 1078, 1091, 1102, 1130, 1133, 1137, 1144, 1145, 1154-1157, 1159, 1160, 1163, 1172, 1191, 1196-1202, 1204-1211, 1213-1216, 1227, 1234, 1241, 1256, 1258, 1268, 1273, 1275, 1276, 1289, 1306, 1307, 1310, 1322, 1323, 1347, 1350, 1353, 1360, 1361, 1363, 1365, 1385, 1387, 1404, 1414, 1431, 1434, 1435, 1447, 1449, 1453, 1460, 1461, 1467, 1473, 1474, 1476, 1478, 1481, 1490, 1491, 1503, 1516, 1517, 1519, 1520, 1530-1533

INDEX OF SPONSORS

National Eye Institute, 1552
National Heart, Lung, and Blood Institute, 0094, 0109, 0434, 0607, 0608, 0617-0619, 0651, 0654, 0655, 0664, 0676, 0689, 0691, 0698-0701, 0718, 0719, 0753, 0755, 0780, 0791-0793, 0825, 0828, 0853, 0873, 0874, 0959, 0962, 0965, 0987, 0998, 1000, 1005-1007, 1041, 1044-1046, 1048, 1053, 1054, 1066, 1076, 1090, 1096, 1100, 1106, 1116, 1117, 1120, 1123, 1127-1129, 1135, 1140, 1142, 1143, 1151, 1189, 1190, 1203, 1214, 1220, 1235, 1277, 1280, 1281, 1305, 1327, 1339, 1356, 1370, 1371, 1378-1380, 1392, 1407, 1409, 1411, 1412, 1415-1419, 1423, 1430, 1432, 1450, 1458, 1498, 1499, 1501, 1502, 1504, 1522, 1523, 0153
National Institute on Aging, 0698, 0834, 0997, 1046
National Institute of Allergy and Infectious Diseases, 0869, 0966, 1497
National Institute of Arthritis, Metabolism, and Digestive Diseases, 0627, 0650, 0668, 0701, 0748, 0762, 1417, 1430
National Institute of Child Health and Human Development, 0610, 0696, 0758, 0772, 0774, 0812, 0958, 0963, 0969, 0987, 1022, 1039, 1040, 1043, 1051, 1052, 1062, 1098, 1113, 1192, 1228, 1229, 1231, 1257, 1262, 1344-1346, 1482, 1525, 1542
National Institute of Dental Research, 0938
National Institute of Environmental Health Sciences, 0687, 1313-1316, 1470
National Institute of General Medical Sciences, 0094, 0672, 0872
National Institute of Neurological and Communicative Disorders and Stroke, 1487
Office on Smoking and Health, 0816, 0972-0974, 1374
U S Environmental Protection Agency, 0618, 0624, 0653, 0682, 0752, 0781, 0783, 0978, 1024, 1063, 1164, 1418, 1472, 1483
U S Veterans Administration, 0608, 0614, 0621-0623, 0629-0633, 0734, 0736, 0738-0748, 0764, 0768, 0769, 0785, 0800-0803, 0807, 0827, 0854, 0856-0858, 0954, 0955, 0964, 0967, 0968, 0970, 1036, 1046, 1094, 1095, 1097, 1106, 1108, 1109, 1119, 1138, 1139, 1147-1149, 1165, 1177, 1179-1186, 1237, 1294-1302, 1332-1337, 1387, 1426-1428, 1436-1441, 1459, 1475, 1484, 1485, 1487, 1488, 1496, 1505, 1534-1538, 1546, 1557, 1558
Uniformed Services University of the Health Sciences, 1020, 1021
Unite de Recherche Pulmonaire, IRSST Quebec, 0103
United Nations Environment Program, 0250
Universidad de Cartagena, 0150
Universidad de Chile Facultad de Medicina, 0140
Universidad de Chile, Sede Oriente, Hospital Del Salvador, 0139
University Hospital, Malmo, Sweden, 0469
University Hospital, Zurich, 0489
University Institute of Social and Preventive Medicine, Switzerland, 0490, 0491
University Medical School, Cracow, Poland, 0438
University of Aarhus, 0166
University of Alabama in Birmingham, 0608
University of Arizona, 0620
University of Arkansas, Health Education Program, 0625
University of Athens, Medical School, 0253, 0255
University of Bergen, 0417
University of Bern, 0493
University of Bombay, 0292
University of Bristol, 0560
University of California, 0702
University of California, Irvine, 0679
University of California, Los Angeles, 0695
University of California, San Diego, School of Medicine, 0701
University of California, San Francisco, 0710, 0711
University of Cape Town Research Fund, 0447
University of Colorado, 0762
University of Colorado School of Medicine, 0758
University of Florida, 0793, 0794, 0795
University of Georgia, 0823, 0824
University of Glasgow, 0588
University of Gothenberg, 0471, 0472, 0475
University of Heidelberg, 0186, 0187, 0188, 0189
University of Helsinki, Finland, 0203
University of Hong Kong, 0258, 0259
University of Illinois, 0852
University of Iowa, 0866
University of Kansas Medical Center, 0877
University of Kentucky, 0889, 0899, 0934, 0942
University of Kuopio, 0204
University of Leeds, 0564
University of London, 0513
University of Louisville, 0940
University of Mainz, Federal Republic of Germany, 0178
University of Maryland, Agricultural Research Station, 1028
University of Maryland Research Foundation, 1026
University of Massachusetts Medical School, 1084, 1086, 1087, 1089, 1092
University of Melbourne, 0032, 0033, 0034, 0036
University of Michigan, 1105, 1106
University of Milan, Italy, 0340
University of Minnesota, 1136
University of Minnesota School of Nursing, 1124
University of Minnesota, School of Public Health, 1121
University of Missouri, 1143
University of Nevada, Reno, 1162
University of New Mexico, 1189
University of New South Wales, School of Community Medicine, 0038
University of New York, Stony Brook, 1278, 1279
University of Newcastle, 0040
University of North Carolina, School of Nursing, 1326
University of Occupational and Environmental Health, 0390
University of Oregon, 1376, 1377
University of Ottawa, 0120
University of Oulu, Finland, 0206-0209, 0211, 0212, 0215, 0216
University of Pennsylvania Hospital, 1408
University of Perugia, Hygiene and Preventive Medicine Institute, 0341
University of Pittsburgh, 1422, 1424, 1425
University of Queensland, 0041
University of San Francisco, 0717
University of Sheffield, 0575
University of South Florida, 1420
University of Southern California, 0718, 0722, 0733
University of Sussex, England, 0579
University of Texas, Cancer Center, 1476, 1477
University of Toledo, College of Pharmacy, 1341
University of Tromso, 0420
University of Turin, 0344
University of Turku, Finland, 0214
University of Utah, School of Medicine, 1492
University of Wales, 0602
University of Washington, 1524, 1525
University of Western Australia, 0008, 0046, 0047
University of Western Ontario, 0134

INDEX OF SPONSORS

University of Wyoming, 1560, 1561
University of Zurich, 0494, 0495
Uranium Industry, 1189

Vanderbilt University, 1457
Verband Deutscher Rentenversicherungstrager, 0191
Vestfold Central Hospital, 0423
Virginia Commonwealth University, 1512, 1513

W.K. Kellogg Foundation, 1069
Washburn University, 0880
Washington State Department of Social and Health Services, 1521, 1539, 1540
Wayne State University, 1112
Wellcome Foundation, London, 0302
Wessex Regional Health Authority, 0578
West Midlands Regional Health Authority, 0516
West of Scotland Cancer Surveillance Unit, 0590, 0591
Western Australia Telethon, 0008
Western Australian Alcohol and Drug Authority, 0006
Western Infirmary, Glasgow, 0585
Western Kentucky University, 0956
William T. Grant Foundation, 0729
Wingate Institute, Israel, 0316
Wisconsin Department of Health and Social Services, 1551
Workers' Compensation Board, New South Wales, 0017
Workers' Compensation Board of Ontario, 0097
World Health Organization, 0010, 0128, 0163, 0173, 0393, 0416, 0470

Yale Comprehensive Cancer Center, 0773
Yale University, Center for Health Studies, 0790
Yale University School of Nursing, 0771
Yale University School of Medicine, 0770
Yokohama City University, 0391
Yorkshire Regional Health Authority, 0512

BLANK PAGE

554.

SUBJECT INDEX

ABORTION
- maternal smoking, alcohol consumption, and conceptus karyotype, relationship, 1257
- pregnancy risk factor, with oral contraceptive use and smoking, 0772

ABSENTEEISM
- age, social class, and smoking relationship, 0543
- days lost for smoking-related illnesses in Finland, economic cost, 0199
- plant workers in Czechoslovakia, smokers vs. nonsmokers, 0153

ACCIDENTS
- (*See also* FIRES)
- motor vehicle accidents and moving violations, smoking habit relationship, 1092

ACETYLCHOLINE
- binding in brain, distinguishing sites from those for nicotine, 1252
- binding in brain of two rat strains, comparison with nicotine, 1250
- binding sites in rat brain and central nervous system, 0910
- high-affinity binding to brain sections, 0983
- nicotine acetylcholine receptors in axon terminals, presence and function, 1479
- nicotine effect on release in human placenta, 1456
- nicotine influence on neuronal expression of receptors, 0616
- nicotine sites of action in rat brain, effect, 1514
- sperm motility enhancement, nicotine effect, 1454
- sulfur compounds and naturally occurring metabolites, protective effect, 1428

Acromegaly *See* **BONE DISEASES**

ADENOCARCINOMA
- (*See also* CARCINOMA)
- males and females in Shanghai, smoking-related risk for lung cancer, 0142
- women in Japan, smoking as risk factor, 0355

Adenoma *See* **NEOPLASMS**

ADOLESCENTS
- advertising format and content effect on cigarette brand preferences, 0695
- advertising influence on perception of smokers and smoking, 0669
- age-related smoking patterns in British students, analysis of contributing factors, 0563
- alcohol, marijuana, cigarettes, and drug use, influence of family, siblings, peers, 1134
- American Cancer Society survey on smoking habits, attitudes, and beliefs, 0690
- antismoking education in secondary schools, Allegheny County, Pennsylvania, 1383
- antismoking education in seventh grade, effect on high school smoking, 1131
- Arab and Jewish in Israel, smoking habits and other health-related behaviors, 0306
- atherosclerosis risk factors, prevention program in Israel, smoking control as component, 0309
- attitudes and viewpoints on smoking among students in Japan, 0353
- attitudes toward school and education, effect on smoking habits in Norway, 0416
- attitudes toward smoking, tobacco production involvement as factor, 0957
- brain tumors, passive smoking as risk factor, 0733
- cancer education programs, Quest and Assegai, comparative evaluation in England, 0532
- cigarette sales by shopkeepers as factor in smoking prevalence, survey, 0516
- clove (kretek) cigarette use, potential health effects, 0106
- diabetic, cardiovascular disease risk factors evaluation, 1417
- difficult temperament as predictor of future marijuana, alcohol, and tobacco use, 1394
- drug abuse, childhood etiologic determinants, 1248
- drug abuse intervention strategies, comparative evaluation, 0727
- drug abuse, parental, sibling, and peer influences, 1246
- drug abuse prevention program promoting healthy alternatives, 1132
- drug, alcohol, and mental health problems, antecedents and mediating factors, 1002
- drug use and abuse in hyperactives, pattern and progression of use, 0673
- early smoking-induced changes in lung function, 0328
- economic, cultural, psychological factors related to smoking in Senegal, 0055
- family influence compared with peer influence on smoking decisions, 1372
- family processes in drug use, 1232
- health education for manual and technical trade students to reduce alcohol and tobacco use, 0478
- health education for smoking cessation, respiratory function tests as added tool, 0330
- health habits and behavior associated with coronary heart disease, longitudinal study, 0959
- health-related behavior, effect on smoking habits, 0305
- high school designated smoking area, effect on smoking incidence, 0611
- high school students in Italy, smoking, alcohol consumption, and drug use, 0342
- hypertension, factors in etiology, 1444
- immunoglobulin levels in 13-year-olds, sex ratio in smokers vs. nonsmokers, 0437
- independence from adult authority and value of education as factors in smoking initiation, 0696
- initiation of smoking, changing patterns in Australia, 0008

References following all entries are to Description Numbers.

SUBJECT INDEX

Japanese junior high school students, smoking habits compared to U.S. data, 0351
low-tar cigarettes and advertising, smoking initiation affect in Great Britain, sex differences, 0505
lung function, active and passive smoking as factors, 0689
lung function, asthma and bronchitis in infancy and childhood, effects with smoking, 0044
lung function, influencing factors, 0222
lung function, students aged 10 to 20 years in Tahiti, smoking as factor, 0497
male, father's role in son's drug use, 1245
marijuana smoking, typography and dose regulation, 0706
mass media antismoking campaign, efficacy by program content, 1323
mothers, smoking habits in England and Wales, 0517
multidimensional antismoking program for seventh graders, long-term efficacy, 0874
oral health in Sweden, smoking habit and snuff use relationship, 0456
parental smoking habits and attitudes, influence on onset of smoking, Paris survey, 0236
patterns and background factors in initiation of smoking, 0531
peer influence on smoking initiation and maintenance, 1113
peer smoking, effect with attitudes, perceived pressure, knowledge of health effects, 1112
periodontal diseases, smokeless tobacco use association, 0756
personal and environmental factors in smoking initiation, 0716
personality dimensions, predictors of adult smoking patterns, 0674
predictors of change in smoking status over time, peer influence, 1542
pregnancy before age 18, stress as factor in outcome, smoking relationship, 0652
pregnant, factors affecting health behavior, 0657
prenatal care for pregnant adolescents, effect on health behaviors, 0658
prevention of smoking programs, 0019 1233
respiratory symptoms and lung function decline, tools for antismoking campaigns, 0226
respiratory symptoms and smoking, relationship, 0240
respiratory system, long-term effects of passive smoke and air pollution exposure, 0435
rural community in Nepal, smoking habits, 0393
school-based antismoking campaign, effectiveness, 0235
science-oriented antismoking curriculum in Israel, effect on behavior and values, 0311
self-efficacy scale as predictor of smoking behavior, 0851
self-reported smoking status on surveys, feasibility study of validity, 0972
seventh grade antismoking program, long-term effects at age 25, 1133
sex differences in smoking habits in Perth, Australia, 0012
sex ratio of smoking habits, 15- to 19-year-olds in New Zealand, 0404
skills training for fifth and sixth graders to prevent smoking in adolescence, 1533
smokeless tobacco use and smoking, sex ratio in 12- to 18-year-olds, 1495
smokeless tobacco use by high school students in Arkansas, sex ratio, 0625
smokeless tobacco use, health education and behavioral training for prevention, 1559
smokeless tobacco use, junior high school students in Cheyenne, Wyoming, vs. smoking, 1561
smoking habits and attitudes of high school seniors, 1104
smoking habits in Athens, changes over 2 years, 0251
smoking habits in Western Australia, effect of educational campaign, 0006
smoking patterns in Australia 1983, 0004
social-psychological health education, effect on smoking initiation, 1062
students aged 13 to 15 in Norway, smoking habits 1985, 0409
students in grades 7 through 12 in Ohio, smoking habits 1971 vs. 1976 vs. 1983, 1341
substance abuse, developmental epidemological studies, 0995
substance abuse prevention program, efficacy of communitywide involvement, 0729
survey of smoking habits for program planning, Manitoba, Canada, 0081
tar/nicotine levels of cigarettes, antismoking campaign relationship, 0232
tobacco tolerance and dependence, comparison with adult smokers, 0705
urban blacks, antecedents of smoking, 1225

Adrenaline *See* **CATECHOLAMINES**

ADVERTISING
adolescent smoking in Senegal, relationship, 0055
adolescents' views of smokers and smoking, influence, 0669
attitudes of children aged 10 to 12 in Australia, predictive of smoking behavior, 0040
Canadian tobacco industry, expenditures vs. antismoking articles in women's magazines, 0090
children's attitudes, effect of viewing "Death in the West", 0709
cigarettes, format and content effect on adolescents' brand preferences, 0695
congressional ban effect on tobacco companies' market shares, 0776
health claims and health images, *Time* magazine 1944-1983, 0845
health warnings on cigarette advertisments, effect of size and page placement, 0014
low-tar cigarettes in Great Britain, adolescent smoking initiation, sex-related effects, 0505
public attitudes toward cigarette promotion in New Zealand, 0403
tobacco industry response to threatened regulation in Western Australia, 0020

AGE FACTORS
(*See also* LONGEVITY)
adolescent and adult smoking patterns in Australia 1983, relationship, 0004
adolescent smoking prevalence in England, for video film development as educational tool, 0563
adolescents 14-16 vs. 16-18 years, smoking effects on lung function, 0328
adults in Perth, Australia, with sex as factors in smoking rates, 0013

SUBJECT INDEX

age antismoking information was given, effects on smoking prevention, 0233
arteriosclerotic lesions, smoking as added risk factor, 0172
cancer incidence in Hawaii, with alcohol consumption, smoking, and race, 0830
cessation of smoking in coronary disease patients, factor with education and occupation, 0299
cessation of smoking intervention by physicians, relationship, 1084
changing consumption patterns in men vs. women, 0008
chronic bronchitis vs. airways obstruction, risk relationship, 1005
cost benefit of smoking cessation, factor with sex and amount smoked, 1079
cutaneous microcirculatory blood flow, 0955
diffuse hypokinesis in male heavy smokers under age 55, 1549
DNA single-strand breaks, with smoking and diet, 0174
fibrinolytic activity of vein walls in women over age 35, smoking effect, 0450
hematology in healthy smokers vs. nonsmokers, effect, 0602
ischemic heart disease patients, effect with second event on smoking behavior, 1088
lung cancer growth rate, factor with sex, histological type, symptoms, smoking, 0319
lung cancer in high-risk men (over 45) who smoke, 1241
lung cancer mortality in Switzerland, sex ratio, 0495
lung function changes in young vocational school students, 0188
males in Switzerland, effect on proportion of cigarette, pipe, and cigar smokers, 0494
males over age 55, lung function changes, spirometry for evaluation, 0279
mortality in smokers over 50 years of age, Denmark, 0168
myocardial infarct in men under 55 years of age, smoking as risk factor, 1040
myocardial infract in women, risk relationship, with smoking, 1039
population subcategories in Canada, variations in smoking over time, factor, 0061
pregnancy outcome effects, with smoking, alcohol consumption, socioeconomic status, 0045
pulmonary deposition and clearance of inhaled particles, effect, 0854
pulmonary tissue response to long-term smoke inhalation in young and old mice, 0895
selenium concentrations in blood, effect with alcohol, oral contraceptives, smoking, 0577
smoking cessation relationship, 1535
stroke in hypertensive patients, factor with smoking, 1485
theophylline metabolism, inhibition and induction, effect with smoking, 0834
Veterans Administration Medical Center employees, smoking habits, 0970
women, smoking as indicator for breast cancer in women aged 40 to 49, 0123

AGING
(*See also* LONGEVITY)
alcohol consumption and smoking in the elderly, 0796
biochemical variables, effect with smoking, alcohol consumption, 0218
circulating pancreatic proteases and aortic aneurysm in aged heavy smokers, 0734
inner city blacks, smoking and perceived health status, relationship, 1175
interrelationships of smoking and the aging process in men vs. women, 0750
lung function changes in nonsmokers, ex-smokers, and smokers, 1419
lung function effects, with smoking, Baltimore longitudinal mortality study, 0997
lung function in Pi MZ phenotype subjects, effect with smoking, 1151
Normative Aging Study in middle-aged men, longitudinal effects, 1046
testosterone and gonadotropins in young, middle-aged, and elderly men, smoking effect, 0054

Agglutinins *See* **ANTIBODIES**

AGRICULTURAL PRACTICES
breeding methods, chemical residue reduction, 1556
catechol and polyphenols in tobacco, effects, 1321
chemical composition of tobacco, effect, 0823
chemical constituents of tobacco, methods for reduction/elimination, 1329
chemical tobacco safety improvement, 1451
dinitroaniline herbicide activity in soil and plant tissues, 0927
disease resistance in tobacco, breeding methods, 0883
fertilizer effects on tobacco leaf components, 0920
genetic method of tar and nicotine reduction, 1331
growth regulators to reduce chemical residues in tobacco, 0805
growth regulators, tobacco sucker control, 1292
inoculation against blue mold disease, 0930
metal levels in tobacco grown on sludge-amended soil, 1030
nitrogen and potassium addition, burley tobacco effects, 0946
nitrogen fertilization and sucker control materials, yield and quality effects, 0826
particulate reduction by selection and breeding, 1330
slow-release nitrogen fertilization, health-related effects, 0944
soil-borne diseases of tobacco, control methods, 0824
soil water stress, effects on growth, yield, and chemical composition, 0953
spraying with trace elements, effect on smoke content, 1311

AIR POLLUTION
aldehydes, chromatographic determination method, 0361
alkylamines and alkylthiols, chromatographic determination method, 0362
asthma and airway function in second and fifth graders, effect with smoking, 0723
automatic, continuous aerosol generating and exposure system for animal experiments, 1264
biological effects of occupational/residental exposure to tobacco smoke, 0194
cancer and other diseases in Shanghai, risk factor with smoking, 0143
cancer mortality relationship in Poland, 0433
carbon monoxide levels in buildings at different time periods, 1400

chronic bronchopulmonary disease, effect in smokers vs. nonsmokers, 0682
environmental factors in acute and chronic obstructive airway diseases, 0618
indoor air quality and energy efficiency, smoking control as reduction technique, 0775
indoor, methods for evaluation and elimination, 0387
indoor, smoking-permitted vs. smoking-restricted buildings, 0099
industrial carcinogens, biological detection, smoking effect, 0402
irritant level of airborne tobacco smoke, formaldehyde, ammonia, 0766
lung cancer risk relationship, 0187
lung function effects, 0049
mortality from chronic diseases, factor with smoking, ionizing radiation, 1410
mutagenicity of enviromental tobacco smoke, 0195
nicotine concentration in daily environment, variability, 0376
occupational, effects with smoking, biological monitoring, 0421
office building, effect of smoking restrictions on air quality, 0068
radiation in dwellings, effect with smoking on lung cancer etiology, 0453
respiratory effects in children, with passive smoke exposure, long-term followup, 0435
respiratory effects in India, smoking as factor, 0293
synergistic effects with cigarette smoke, cell culture studies, 0064
urban vs. rural residence, factor with smoking on chronic bronchitis incidence, 0427
ventilation of tobacco smoke in real rooms, methods, 0373
ventilation requirements to reduce passive smoking risks, 0783

ALCOHOL CONSUMPTION
adolescents, antecedents and mediating factors, longitudinal study, 1002
adolescents, attitudes and behavior of family, siblings, peers as factors, 1134
adolescents, prevention/intervention programs, 0727
adolescents in manual and technical trade schools, health education for control, 0478
adolescents, relationship with difficult temperament in young adulthood, 1394
adults in Ireland, relationship with smoking, 0295
Arab and Jewish adolescents in Israel, with smoking and other health-related behaviors, 0306
audiovisual slide presentation on health hazards during pregnancy, 0082
benzo(*a*)pyrene metabolism in oral tissue microsomes of smokers and hamsters, effect, 1253
benzo(*a*)pyrene monooxygenase activity in rats, effect with tobacco pyrolysates, 1293
beta-carotene and retinol deficiency in buccal mucosa of heavy smokers and drinkers, 0066
cancer patients, epidemiology data system, 1269
cancer risk factor, with smoking, 0231
cardiovascular morbidity and mortality, risk pathway determination, with smoking, 0700
cessation of smoking in recovering alcoholics, characteristics of quitters vs. recidivists, 1527
childhood and adolescent emotional and adjustment characteristics as predictors, 1393
children, Primary Health Curriculum Project, followup study, 1524
chronic bronchitis vs. airways obstruction, risk relationship, 1005
coffee and tea consumption, relationship, 0134
communitywide intervention for alcohol and tobacco abuse in under-25-year-olds, 0859
coronary artery disease patients, baseline characteristics in 5-year treatment program, 1416
diabetic adolescents, cardiovascular disease risk evaluation, 1417
drug abuse research, relationship with smoking and coffee drinking, 0991
elderly persons, comparison with smoking habits, 0796
elderly persons, effect on biochemical variables, with smoking, 0218
emergency medical technicians, occupational stress as factor, 1362
endoscopic survey for esophageal dysplasia in patients with history of alcohol use, 0856
fertility and smoking relationship in Danish women, 0161
glaucoma risk relationship in blacks vs. whites, 0999
head and neck cancer etiology, effect with tobacco-related carcinogens, 1347
health promotion program for villages in Finland, 0205
Healthstyles program to promote health-enhancing behavior, 0074
heart disease risk factor, with smoking, Australian survey 1980, 0016
high school students in Arkansas, with smokeless tobacco use, 0625
high school students in Italy, smoking habit relationship, 0342
high school students, related administrative problems, with smoking and marijuana use, 0648
inflammatory response in smokers, suppression effect, 0913
inner-city junior high school students, perceived neighborhood setting as factor, 0798
intravenous nicotine self-administration in rhesus monkeys, effects, 0357
Japanese-American men, factor with smoking in diabetes mellitus, 1528
Japanese men born and living in Hawaii, coronary disease risk relationship, 0828
large bowel cancer risk relationship, with tobacco use and diet, 0033
laryngeal and lung cancer risk factor, with smoking, 0296
laryngeal cancer risk relationship, with occupation and smoking, 0347
liver cancer risk relationship, with hepatitis infection, smoking, 0732
lung cancer risk relationship, 0034
male subfertility, factor with smoking, 0774
middle-aged men in Sweden, heart disease and cancer mortality risk, with smoking, 0474
morbidity and mortality relationship in Barbados, 0053
morbidity risk in smokers vs. nonsmokers, genetic and epidemiologic differences effect, 0998
mortality 1980, with smoking, drug abuse, 0971
myocardial infarct in men under 55 years of age, risk with smoking, 1040
nasopharyngeal neoplasms, risk factor with occupational exposures and smoking, 0720
nitrosamines, cocarcinogenicity in rats, 1204
noise-exposed workers in Pittsburgh, 1418

SUBJECT INDEX

Normative Aging Study n middle-aged men, longitudinal effects, 1046
North Dakota telephone risk factor prevalence survey, 1338
oral and esophageal cancer risk relationship, with diet and smoking, 0032
oral and pharyngeal cancer risk factor, with smoking, 1183
oral cancer risk relationship, 0345
oral, laryngeal, esophageal cancers, risk factor with smoking, diet, occupation, dental hygiene, 1520
oral leukoplakia risk relationship, 1459
pancreatic, bile-duct, and gallbladder cancer risk relationship, with tobacco use, 0246
pancreatic cancer, risk factor with chemical exposures and smoking, 0467
pancreatic cancer risk relationship, with diet, smoking, and family history, 0036
parotid gland cancer, factor with x-ray exposure and smoking, 0721
physicians in Japan, mortality relationship with smoking, long-term followup, 0390
pregnant women, effect with smoking, 0045 1262
premenopausal women, effect with exercise and smoking on high density lipoprotein cholesterol, 0934
psychiatric patients, role in early mortality, 1095
puffing behavior of inhalers vs. noninhalers, relationship, 0485
reliability of long-term recall in prevention programs, 0661
renal cell carcinoma, risk relationship, 1363
secondary school students in Australia, survey, 0005
selenium and vitamin E concentrations in serum, effect with smoking, 0578
selenium concentrations in blood, effect with smoking, 0577
small town population in New Zealand, fourth cardiovascular risk factor survey, 0405
smoking behavior during alcohol withdrawal, 1302
smoking cessation relationship, 1535
stress modification in black and white household populations, 1265
submucous fibrosis and oral carcinoma in South African Indians, factor with betel nut chewing, 0446
temporal variations in Torino, Italy, with smoking habits, 0346
ulcerative colitis risk relationship, 1537
Washington State risk control survey, 1540

ALCOHOLS
tobacco smoke carcinogens, inhibition of localization in tumor sites, 0936

ALDEHYDES
(*See also* FORMALDEHYDE)
chromatographic determination method for levels in polluted air, 0361
mainstream and sidestream smoke, quantification method, 1211
sulfur compounds, protective effect against cigarette smoke toxicants in rats, 1428

ALKALOIDS, TOBACCO
(*See also* COTININE, NORNICOTINE)
chemical analysis of leaf constituents, 0950
cross breeding of burley with Maryland cultivar for low-level strain development, 1028
cytisine, generalization in rats trained to discriminate low dose of nicotine, 0521
nicotine, nornicotine, and minor species level determinations, 0943
teratogenicity, 1494
volatile and particulate phases of cigarette or tobacco smoke, determination, 0822

ALLERGY
cigarette smoke and tobacco extracts, asthma relationship, 0966
nicotine reaction in seborrhoeic dermatitis, 0247
snow crab processing workers, occupational exposure and smoking as factors, 0084

ALTITUDE
cardiovascular effects in rats, with/without carbon monoxide exposure, 1469

AMBLYOPIA, TOBACCO
rhodanese activity, inheritance, 0556

AMIDES
assay methodology for detection in tobacco, smoke, and saliva of tobacco users, 1211

AMINES
(*See also* AROMATIC AMINES)
aliphatic and aromatic, determination in cigarette or tobacco smoke, 0822
alkylamines and alkylthiols in polluted air, chromatographic determination method, 0362
mecamylamine, blocking of nicotine cue in rats, 0521

AMINO ACIDS
acetylcholine-stimulated release in placenta, nicotine effect, 1456
tobacco pyrolysate, mutagenic activity in rat lung, effect with alcohol consumption, 1293
umbilical arteries and veins, levels in smokers vs. nonsmokers, 1455

ANABASINE
(*See also* ALKALOIDS, TOBACCO)
generalization in rats trained to discriminate low dose of nicotine, 0521
lanka tobacco of India, levels, 0268

Aneurysm *See* **VASCULAR DISEASES**

ANGINA PECTORIS
(*See also* CORONARY DISEASE)
health decision model as basis for cessation program for angina patients, 1496
pipe and cigar smoking by patients, long-term effects, 0301
short-term prognosis in smokers, 0298

Anoxia *See* **HYPOXIA**

ANTIBODIES
(*See also* IMMUNE SYSTEM)

benzo(*a*)pyrene diol epoxide, monoclonal antibodies to detect hemoglobin levels, 1230
blood levels as marker for early detection of lung cancer, 0116
extrinsic allergic alveolitis, smoking effect on production, 0365
IgG response to tobacco smoke, smokers vs. nonsmokers, 0028
Micropolyspora faeni serum antibodies in farmers, smokers vs nonsmokers, 0366

ANTIGEN-ANTIBODY REACTIONS
(*See also* IMMUNE SYSTEM)
cigarette smoke exposure effects in rats, 0915

ANTIGENS
(*See also* IMMUNE SYSTEM)
ABH in lungs, relationship of secretor status and lung function in smokers vs. nonsmokers, 0546
carcinoembryonic antigen assay for monitoring patients with head and neck neoplasms, 1185
cell mediated immunity against tobacco antigens in thromboangiitis obliterans patients, 0274
respiratory tract glycoproteins as carcinoembryonic antigen markers, 0769
T-independent and T-dependent in mice, smoke exposure effects on antibody response, 0915
tobacco smoke extract vs. extracts of other solanaceous plants, 0028

ANTISMOKING CAMPAIGNS
(*See also* HEALTH EDUCATION, PREVENTION OF SMOKING; SMOKING CONTROL PROGRAMS)
ACS, FreshStart cessation of smoking program, 1194
adolescents, respiratory symptoms and lung function decline as tools, 0226
age antismoking information was given, effects on smoking prevention, 0233
Allegheny County, Pennsylvania, antismoking education program, 1383
AMA, Oregon program for health professionals, 1366
Australia, pilot smoking cessation programs in South Australia, 0019
Australian "Quit For Life," evaluation and results, 0009
California, Risk and Youth: Smoking Project in elementary and junior high schools, 0675
Canada, school-based program development, 0127
Canada, Smoke-Free Spaces for Kids program to promote nonsmoking as the norm, 0069
China, smoking cessation program for factory workers, 0148
communitywide intervention for alcohol and tobacco abuse in under-25-year-olds, 0859
education program for fifth grade students in Moscow, 0502
Egypt, evaluation of various approaches, 0173
England and Wales, recommendations for prevention policies in district health authorities, 0553
England, trade unions support of program for control of workplace smoking, 0523
Finland, economic simulation model for analyzing policy options, 0199
Finland, health promotion program for villages, 0205
Finland, televised smoking cessation program, efficacy, 0201
hospital antismoking policy formation and implementation, 1072
India, multifaceted program against tobacco use, 0286
interagency smoking cessation program for pregnant women, 0634
Iowa public schools, multidimensional smoking education program for seventh graders, 0874
Israel, community program for reduction in smoking, 10-year followup, 0312
Israel, multifacted program for health education, smoking cessation, 0304
Israeli kibbutz, efficacy of educational materials and physician's advice for cessation, 0313
Italy, national education program for high school students, 0336
Italy, program to increase awareness among health professionals, 0335
Kansas, Project VOTE to promote workplace smoking policy, 0876
Kaunas-Rotterdam Intervention Study for cardiovascular disease risk reduction, 0397
Latrobe Valley (Canada), community smoking control project, 4-year evaluation, 0079
mass media program for adolescents, comparison of varied content, 1323
Minnesota Heart Health Program, community-based interventions, 1135
Minnesota Heart Health Program for cardiovascular disease risk reduction through education, 1120
the Netherlands, prevention of smoking in school children aged 10 to 15 years, 0398
northern California, two communities participate in smoking cessation contest, 0664
nurse practitioners, role, 0771
Philadelphia, for public and private school students, women, general public, 1395
physicians' smoking cessation program, efficacy of training with/without nicotine gum, 1137
school-based, role-playing intervention for fifth and sixth grades, effectiveness, 1103
secondary schools, teacher-led, effectiveness, 0235
social-psychological intervention, effect on adolescent smoking initiation, 1062
southwest Texas, media and community programs for cessation/prevention, 1481
tar/nicotine levels of adolescent smokers and type of campaign, relationship, 0232
UICC worldwide cancer prevention project, 0003
veterans' hospital, response to positive vs. negative approaches, 0967
Washburn University smoking and health fair, 0880
Western Australia, effect on smoking initiation among adolescents, 0006
Western Australia, four-phase media campaign to promote cessation, efficacy, 0015
worksite educational, self-help program, 1171

ANTISMOKING MATERIALS
activity book on smoking and health for fourth and fifth grades, 0122
American Lung Association self-help manuals for smoking cessation, efficacy, 0493

SUBJECT INDEX

audiovisual slide presentation on health hazards during pregnancy, 0082
bibliography on involuntary (passive) smoking, 0710
booklet in conjunction with televised smoking cessation program in Great Britain, 0507
booklet on smoking cessation, efficacy with physician advice, with/without nicotine gum, 0593
classroom curriculum for prevention of smoking, alcohol use, and drug abuse in adolescents, 1509
computerized cessation program materials by mail, efficacy, 1237
day-by-day instruction manual for cessation of smoking in 20 days, 0104
handbook for physicians for conducting smoking cessation program with patients, 0038
health education materials emphasizing more immediate effects of smoking, Israel, 0304
information kit to increase smoke-free areas in workplaces, 0063
instructional materials on lifetime tobacco use and disease risk relationship, 1037
leaflet on cessation, efficacy with physician's counseling, 0572
manual for school-based prevention program, 0127
messages, source credibility determination in drug education, 0860
newpaper articles and posters in Israeli kibbutz, efficacy, 0313
pamphlet and bibliography of manuals for self-quitters, long-term evaluation of efficacy, 1322
pamphlet of health effects of passive smoking, 1539
poster campaign in Egypt, efficacy, 0173
posters, printed materials for military enlisted personnel in Italy, 0334
Project VOTE (Kansas), kit of materials to promote workplace smoking policy, 0876
revision of "Smoking and Health Experiments, Demonstrations, and Exhibits", 1374
school-based program, effect on smoking initiation, 0131
self-administered relapse prevention materials, efficacy with/without nicotine gum, 0662
self-help guide, efficacy with/without added assistance, 1193
self-help manual, efficacy with/without nicotine gum in pulmonary disease patients, 0137
signs, posters, print materials in hospitals, efficacy, 0967
slide/tape programs for adults to promote smoking cessation, 0645
stories and activities for young children, use by physician for prevention of smoking, 1476
taped messages in 24-hour reduced stimulation smoking cessation program, efficacy, 1508
UICC manuals for lung cancer prevention, 0003
videotapes at workplaces for smoking cessation, efficacy, 0504

ANTITRYPSIN LEVELS
acute smoking effects on lung lavage fluid levels and activity, 0115
bronchoalveolar lavage fluid, 1148
cab drivers, respiratory disease relationship, 0241
ceruloplasmin and ferrous iron transferrin levels, relationship, 1297
phenotype Pi, concentrations in smokers vs. nonsmokers, 0224
saliva of 13-year-olds, α_1-antitrypsin levels in smokers vs. nonsmokers, 0437

ANXIETY
alcohol withdrawal, prolactin, and nicotine effects, 1302
behavioral marker of cholinergic/β-endorphin activity from nicotine intake, 0767
cessation of smoking, factor in success of self-quitters, 0325
clonidine effects during smoking withdrawal, 1488
microcomputer program for reduction, 1075
nicotine effects in rats, 1511
Normative Aging Study in middle-aged men, longitudinal effects, 1046
veterans in self-help smoking cessation program, effect on outcome, 1106

AORTA
adhesion and diapedesis of monocytes in smoke-exposed rats, factor in arteriosclerosis, 1090
endothelial cell changes following smoke inhalation in rats, 0535
endothelial cell damage and prostacyclin production in rats, nicotine effects, 0537
fetal, maternal smoking effect on pulse wave volume, 0469

Aortic aneurysm *See* **VASCULAR DISEASES**

ARECA
mucosa of hamster cheek pouch, ultrastructural and histological effects, 0498

ARECA CHEWING
(*See also* TOBACCO CHEWING)
carcinogen formation, 1196
submucous fibrosis in South African Indians, risk relationship, 0446

AROMATIC AMINES
(*See also* AMINES)
cigarette smoke condensate, synergistic effects, 0395
tobacco carcinogenesis, role, 1207
tobacco nitrate effect on formation in cigarette smoke, 1202

AROMATIC HYDROCARBON CONTENT
bidi, cigarette, chutta, chillum, and hookah tobacco smoke, 0266

AROMATIC HYDROCARBONS
(*See also* **BENZ(*A*)ANTHRACENES; METHYLCHOLANTHRENE; BENZO(*A*)PYRENE**)
activation and detoxification of polycyclics in tobacco condensate, 0354
atherosclerotic lesions in avian species, role in etiology, 1526
biological carcinogenic effects of cocarcinogens and tumor promoters, 0862
bronchial susceptibility, effect of B_{12} and folate deficiency in smokers, 0606
cigarette smoke components, effect on variation and activity of cytochrome P-450 complex, 0443
cigarette smoke compounds, aryl hydrocarbon hydroxylase induction in rats, 0441
dihydrodiol derivatives, metabolic fate and toxicology, 0190
epoxide hydrolase activation in liver, role in carcinogenesis, 1157

SUBJECT INDEX

gas and particulate phases of cigarette smoke, carbon filtration effect on carcinogenicity, 0175
genetically controlled responsiveness in cigarette smoke toxicity in mice, 0212
7H-dibenzo(*c, g*)carbazole, polynucleotides and DNA binding, 1359
polycyclic hydrocarbon metabolism and carcinogenesis, 1156
structure—activity relationships and relative carcinogenicity, 1365
3-methylcholene, lung cancer induction relationship in mice, 0717

ARRHYTHMIA
(*See also* HEART DISEASES; HEART FUNCTION)
cadmium-enriched cigarettes, vascular reactivity and arrhythmogenic threshold changes in rats, 0912
smoking relationship, 0463

ARSENIC
chromosome aberration frequencies in hamster cells, synergism with cigarette smoke, 0064
tobacco levels in Western vs. Chinese brands, 0185

ARTERIAL DISEASES
(*See also* ARTERIOSCLEROSIS; THROMBOANGIITIS OBLITERANS; VASCULAR DISEASES)
aneurysm, enzyme activity and smoking as factors in the elderly, 0734
carotid artery atherosclerosis, smoking effect, 1115
coronary artery bypass graft surgery patients, smoking cessation and locus of control, 1332
coronary artery disease, individual, organizational, extra-organizational factors, 1442
males with erectile dysfunction risk relationship, 0765
small and large vessel peripheral arterial disease, risk factors, 0699
thromboangiitis obliterans, cell-mediated immunity against tobacco antigens in patients, 0274

ARTERIES
(*See also* AORTA; BLOOD VESSELS)
atherome plaques in arterial wall, nicotine effects, 0500
blood pressure regulation in rats, smoke inhalation effect, 0904
coronary bypass patients, diet therapy with/without drugs, effects in nonsmokers, 0719
fistulas used in renal dialysis, smoking effect on long-term patency, 0595
infants, maternal smoking effect on intimal layer of coronary arteries, 0193
maternal O_2 transport at high altitudes, smoking effects, 0755
mitochondrial proliferation in umbilical arteries of newborns, maternal smoking effect, 0171
nicotine effect on main and digital vessels, 0842
pinocystolic activity in smokers vs. nonsmokers, 0170
platelet reactivity in plasma following smoking, 0535
umbilical, inhibitory effect of nicotine on amino acid uptake in smokers, 1455

ARTERIOSCLEROSIS
(*See also* ARTERIAL DISEASES; CORONARY DISEASE)
adhesion and diapedesis of monocytes as mechanism, smoke inhalation effects in rats, 1090
arterial wall hypoxia, carbon monoxide-induced, effect on etiology, 0839
carotid artery, smoking effect, 1115
cessation of smoking effect on risk factors, 0119
changing incidence in long-term smoke-exposed dogs, 1178
cigarette smoke constituents, mechanisms of action in atherogenic process, 1203
coronary bypass patients, effect of drug/no-drug treatment in nonsmokers, 0719
cutaneous blood flow in smoking and nonsmoking patients, 0955
experimental induction with streptozotocin and high-cholesterol diet in rats, 0745
Kuopio Ischaemic Heart Disease Risk Factor Study, 0204
mutagenicity of cigarette smoke, 1522
physiological and biochemical participation of smoking in experimental disease in rabbits, 0372
prevention program for children and adolescents in Israel, smoking control as component, 0309
surgery patients, smoking habits, 0172

Arteriosclerosis, coronary *See* CORONARY DISEASE

Aryl amines *See* AROMATIC AMINES

ARYL HYDROCARBON HYDROXYLASE
aromatic hydrocarbons in cigarette smoke, effects in rats, 0441
chrysotile fibers and 3-methylcholanthrene inducement in mice, 0430
mainstream and sidestream smoke condensates, effect in rat liver and lung, 0343
monoclonal antibodies to methycholanthrene-P-450, inhibition of activity in human placenta, 0990
placental detoxification system, activity in response to smoke, 0758

Aryl hydrocarbons *See* AROMATIC HYDROCARBONS

ASBESTOS
biomarkers for risk index in exposed shipyard workers, 0678
cancer prevention with retinol and beta-carotene in workers with asbestos-related lung disease, 1531
cancer risk in exposed shipyard workers, smoking relationship, 0831
chrysotile fibers, aryl hydrocarbon hydroxylase inducement in mice, 0430
epithelial hyperplasia and metaplasia of airways in hamsters, effect with/without benzo(*a*)pyrene, 0358
exposure as factor in mesothelioma etiology, with smoking, 0318
exposure effects on saltpeter workers, with smoking, 0413
lung cancer mortality in exposed workers, smoking relationship, 0565
lung diseases and immunologic abnormalities in exposed workers, smoking as factor, 0429
lung function in families of workers, effect with smoking in Los Angeles, 0722
morbidity and mortality of exposed workers, smoking relationship, 0515
pleural plaques in exposed workers, smoking relationship, 1389
psychological comparison of asbestos workers with mesothelioma patients, 1223

SUBJECT INDEX

questionnaires as screening instruments for bronchitis in workers, 0460
respiratory disease, occupational exposure and smoking as factors, 0017

ASBESTOSIS
(*See also* OCCUPATIONAL DISEASES; PNEUMOCONIOSIS)
saltpeter workers, effect of dust and smoking on morbidity and mortality, 0413

Ascorbic acid *See* **VITAMIN C**

ASTHMA
(*See also* LUNG DISEASES)
allergy to tobacco smoke products as factor, 0966
children, passive smoking effects, 0076
children, smoking effect on pharmacologic management, 0869
diurnal variations in airway obstruction in patients, smoking effect, 0512
environmental conditions, effect with smoking, 0618
histamine and leukotrienes as mediators, smoking effect, 0853
infancy and childhood, long-term effect with smoking on lung function, 0044
infants with bronchiolitis, relationship, passive smoking as risk factor, 0023
longitudinal study of 7-year-old patients, disease and smoking habit data at age 21, 0022
lung function response to passive smoke in nonsmokers, influence of suggestibility, 0126
reversible and fixed airway obstruction in patients, smoking and social class as factors, 0511
second and fifth grade students, smoking and air pollution effects, 0723
snow crab processing workers, occupational exposure and smoking as factors, 0084

Atelectasis *See* **LUNG DISEASES**

Atherosclerosis *See* **ARTERIOSCLEROSIS**

ATTITUDES
(*See also* BEHAVIOR, HUMAN)
adolescent smoking, family vs. peers, effect, 1372
adolescents and adults in California, smoking attitudes, beliefs, and behavior, 0690
adolescents in Israel toward smoking, intervention program effect, 0310
adolescents toward smoking, effect with perceived peer pressure, 1112
adolescents, value approach for prevention/reduction of smoking, 1541
adolescents' views of smokers and smoking, advertising influence, 0669
adults in Ireland toward smoking, social and cultural influences, 0295
anger expressed in group phychotherapy, with or without smoking prohibitions, 1301
antismoking campaign in Egypt, effect of various approaches, 0173
Biofeedback Smoking Education Program, effect on attitudes of smokers and nonsmokers, 0835
change procedures to enhance maintenance of abstinence, 0850
children aged 10 to 12 toward cigarette advertising, predictive of smoking behavior, 0040
children and adolescents in northern England, smoking habit relationship, 0531
children in grades 4, 5, and 6, program to develop antismoking attitudes, 1015
children toward cigarette advertising, effect of viewing "Death in the West", 0709
cigarette promotion and restraints on smoking in New Zealand, public attitudes, 0403
college undergraduates in the midwest about smokeless tobacco use, 0844
coronary disease patients, effect of hostility and smoking on future events and mortality, 1305
current vs. ex-smokers about smoking, differences, 0552
elementary schoolchildren and students in Japan, viewpoints on smoking, 0353
employees and employers on industrial smoking cessation schemes, 0526
employees who watched antismoking videotapes at workplace, 0504
ex-smokers, abstinence maintenance attitudes in males vs. females, 0525
factory workers in China, smokers' opinions about smoking, 0148
family, siblings, peers of adolescents, influence on substance use/abuse, 1134
fifth and sixth grade students, intervention program effect, 1103
fourth and fifth grade students toward smoking, perceived attitudes of friends, parents, 1501
health- and smoking-related in adolescents, effect on initiation of smoking, 0696
health effects of smoking, effect of smoking behavior, 0562
health professionals in Italy toward smoking, 0335
Healthstyles program to promote health-enhancing behavior, 0074
high school seniors, changes over time, 1104
high school students in Israel toward smoking, effect of science-oriented program, 0311
hospital patients and staff, antismoking policy formation and implementation, 1072
junior high students, effect on classroom smoking prevention program, 0724
media campaign for cessation of smoking in Western Australia, smokers' attitudes, 0015
medical services workers in China toward smoking, 0149
medical students in England, changes in attitudes toward smoking from 1972 to 1981, 0558
multidimensional antismoking program for seventh grade students, effect, 0874
nurse practitioners toward antismoking advice for patients, 0771
nurses in North Carolina, smokers vs. ex-smokers vs. nonsmokers, 1326
nurses in South Africa about smoking in public places, 0447
nurses, perception as health educators among smokers vs. nonsmokers, 0773
nurses, smoking habit relationship, 1087

parents and peer groups of schoolchildren in Dublin, smoking habit relationship, 0294
participants in group cessation program, quitters vs. continuing smokers, 0644
paternal personality and childrearing practices, effect on daughter's drug and tobacco use, 1222
physicians, effect on cessation of smoking in patients, 1083
positive vs. negative approaches to discourage smoking in hospitals, effects, 0967
pregnant women toward breast feeding, smoking habit relationship, 0041
preschool children, health education effect over time, 1482
rural and urban residents of Ontario, Canada, smoking restrictions in public places, 0138
schoolchildren aged 11, 13, and 15 in Norway toward education, smoking habit relationship, 0416
seventh graders, parental involvement in drug abuse prevention program, effect, 0726
seventh graders, smoking prevention curriculum, factor in efficacy, 1234
shopkeepers in England toward adolescent smoking, effect on sales, 0516
smoking cessation effects in group sessions, 0741
smoking-related in Australia, "Quit For Life" campaign impact, 0009
social network members, influence on smoking cessation outcome, 1162
students in Argentinian technical school toward smoking, 0002
students, parents, teachers, effect of involvement with tobacco production, 0957
teachers in primary vs. secondary schools in Wales toward smoking, 0597
tobacco and alcohol intervention program for under-25-year-olds, factor, 0859
university hospital staff, faculty, and students toward smoking cessation programs, 0207
viewers of televised series in Great Britain, 0507
workplace smoking restrictions, smokers vs. nonsmokers, 1351
worldwide policies on smoking in hospitals, attitudes and practices, 0010

Automobile accidents *See* **ACCIDENTS**

AVERSIVE THERAPY
cessation of smoking treatment, efficacy, 0639
effectiveness in a hospital setting, 0968
long-term outcome efficacy vs. nonaversive treatment, 0867
rapid smoking as adjunct to nicotine gum for cessation, efficacy, 0027

Avoidance learning *See* **AVERSIVE THERAPY**

BACTERIA
bronchial mucosa specimens vs. bronchial washings, values and limits for bacteriological study, 0426
chronic lung disease patients, adherence in tracheal cells, smoking effect, 1249
Legionella pneumophila, animal model, smoking effects, 1497
microorganism alteration of tobacco leaf components, chemical means, 0947
nitrate-reducing, leaf-curing effects, 0881
nitrate reduction and nitrile production in tobacco, 0951
oral, smokeless tobacco extract effects on growth, 1029
oropharyngeal, in vitro effects of cigarette smoke, 1168
recombinant DNA techniques for tobacco protein reduction, 1032
smoke constituent effects, 1304
ureaplasmas, colonization in placenta, neonatal effects, 1051

Bagassosis *See* **PNEUMOCONIOSIS**

BEHAVIOR, ANIMAL
(*See also* MOTIVATION)
carbon monoxide exposure during gestation, behavioral evidence of effect, 1003
chronic nicotine exposure effects in rats, 1560
cocaine and nicotine self-administration, fixed- vs. progressive schedule effect in dogs, 1013
drug administration, pharmacological and psychological mechanisms of subjective effects, 1406
lever response in nicotine-exposed rats, subjective symptoms of withdrawal, 1468
locomotor responses in rats, hippocampal 5-HT lesions and nicotine administration effects, 0587
locomotor stimulation, possible therapeutic use of long-acting central nicotinic antagonist, 0983
maintenance and suppression by intravenous nicotine injections in squirrel monkeys, 1055
nicotine and psychotropic drugs, interactive effects, 0357
nicotine, effect in primates, 0817
nicotine-induced behavioral and physiological response in mice, genetics of tolerance, 0757
nicotine intake and smoking effects in monkeys, 0356
nicotine, intravenous administration effects in rabbits, 1021
nicotine, nornicotine, cotinine, cocaine, norcocaine, effect on responding in dogs, 1014
nicotine, reinforcing and aversive effects in rats, specificity of nicotine cue, 0521
nicotine reinforcing properties, effects in rats, 0909
pharmacological and environmental factors in control by nicotine in squirrel monkeys, 1057
psychopharmacology of nicotine sulfate in rats with nucleus basalis magnocellularis lesions, 1562
self-administration in rats as model of tobacco dependence, 0249
steroid hormonal and nicotine effects in mice, 0818

BEHAVIOR, HUMAN
(*See also* ATTITUDES, MOTIVATION, PERSONALITY, SMOKING CHARACTERISTICS)
abstinence training for cessation of smoking, efficacy in long-term smokers, 1139
achievement motivation in young women, smoking habit relationship, 1384
addicted vs. environmentally influenced smokers, effect of treatment type on cessation, 0866
adolescent drug abuse, determinants, 0995

SUBJECT INDEX

adolescent drug abuse, intervention strategies, 0727
adolescent smoking behavior, self-efficacy scale as predictor, 0851
adolescent smoking, peer influence on initiation and/or maintenance, 1113
adolescents, assertiveness training to resist pressures to smoke, 1161
adolescents, effects of social-psychological intervention on smoking initiation, 1062
adolescents in Israel, health-related behaviors and smoking habit, 0305
adolescents, validity of self-reported smoking status on surveys, 0972
adults in Finland, lifestyle factors and disease incidence, relationship, 0201
adults in Ireland, social and cultural influences on smoking habits, 0295
alcohol consumption and smoking by emergency medical technicians, occupational stress as factor, 1362
attitudes, beliefs, and smoking behavior, American Cancer Society California survey, 0690
aversive vs. nonaversive treatment for smoking cessation, group cohesiveness as factor, 0857
baseline characteristics as predictors of success in smoking cessation, 0038
biobehavioral markers of β-endorphin reinforcement of smoking, 0767
cardiovascular disease risk factors in nurses, with smoking, 1054
causal attributions for behavior in smoking cessation clinic participants, 1368
cessation of smoking, efficacy of modification programs, 0109 1170
cessation of smoking, health and self-efficacy beliefs as success factors, 1457
cessation of smoking, perceived personal vulnerability as factor, 1109
characteristics of quitters vs. continuing smokers in group cessation program, 0644
chewing tobacco users, modification for cessation, efficacy, 0749
child at age 10, parental smoking relationship, 1192
childhood and adolescent characteristics as predictors of smoking, 1393
children aged 10 to 12, factors associated with changes in smoking behavior, 0040
children and adolescents for atherosclerosis prevention, modification program, 0309
children and adolescents in "Know Your Body" program, efficacy for smoking prevention, 1214
children and adolescents, predictors of change in smoking status over time, 1542
children at age 7, effects of maternal smoking during pregnancy, 1391
children grades K-6, development of beliefs and attitudes toward smoking, 0779
children, health habits and behavior, smoking in coronary disease risk study, 0959
children of substance-abusing families, prevention/intervention services, 1493
cigarette consumption level effect on cerebral blood flow, disease risk, 1487
cocaine users, interaction with alcohol, tobacco, marijuana, and diazepam use, 0847
coffee consumption and smoking, relationship, 0996
coffee consumption, smoking and other predictive factors, 0134
cognitive, affective, and behavioral changes in 16-year-olds, cancer education efficacy, 0532
community-wide education program to reduce lifestyle heart disease risk factors, 1430
competition and prizes in worksite smoking cessation program, participation effect, 1339
complex problem-solving tasks, performance by smokers vs. ex-smokers vs. nonsmokers, 1066
compliance with instructions for use of nicotine gum, factors in self-administration, 1126
conferences to explore issues in smoking behavior research and policy development, 1068
coping skills training, efficacy for prevention/cessation, 0607
coronary disease patients, effect of hostility and smoking on future events and mortality, 1305
coronary disease risk factors, 5-year followup study, 1277
coronary-prone middle-aged men, modification techniques for smoking cessation, 1100
counseling on modification for smoking cessation, 0118
culturally based model of tobacco use, 1173
demography of smoking, designing and evaluating public policies for cessation or prevention, 1070
diet, alcohol use, smoking as heart disease risk factors, Australian survey 1980, 0016
drug abuse by inner-city junior high school students, neighborhood setting as factor, 0798
drug and mental health problems in adolescents, antecedents and mediating factors, 1002
drug use and abuse in hyperactive adolescents, treatment as children as factor, 0673
everyday stressors as factors in ex-smokers who relapse, 0799
family effectiveness training for prevention of drug abuse in children, 0797
five-stage model of change for self-help smoking cessation, 1434
Framingham Offspring Study, Cycle III, 1041
gradual withdrawal smoking cessation program, characteristics of quitters vs. recidivists, 0836
health behavior inventory for corporate settings to encourage employee wellness, 1243
health practices and educational efforts of general practitioners, nurses, educators, 0401
health-related, measurement of strategies and behaviors as prevention index, 1396
Healthstyles program to promote health enhancing behavior, 0074
high arousal vs. low arousal situation smokers, reactions to first cigarette of the day, 0579
high-risk youth, sixth grade curriculum for prevention of smoking, efficacy, 1532
high school students, seventh grade prevention program effect on smoking habits, 1131
hospitalized alcoholics, puffing patterns following smoking restriction, 1427
immunoglobulin E, patterns in rare vs. light vs. heavy smokers, 0958
individual's smoking habit, influence on family, 1395

SUBJECT INDEX

inoperable cancer patients, treatment program to change self-destructive habits, 0785
Institute for the Study of Smoking Behavior and Policy, Harvard University, 1069
institutional vs. community nurses in South Africa, differences in smoking habits, 0447
junior and senior high school students effect of multiyear smoking prevention program, 1519
junior high school students, skills training to prevent smokeless tobacco use, 1559
junior high students, intentions to smoke effect on classroom prevention program efficacy, 0724
Know Your Body program for grades 4-6, behavior modification for coronary disease prevention, 0780
Lifecycle model of preventive health services, cessation of smoking for risk reduction, 1242
lung clinic patients, modification program for smoking cessation to qualify for treatment, 0179
male subfertility, smoking and lifestyle factors, survey, 0774
male vs. female smoking habits, underlying factors and effect of clean indoor air laws, 1166
mass media campaign for reinforcement of modification clinic for smoking cessation, efficacy, 1505
middle-aged male myocardial infarct patients, rehabilitation program effect, 0399
monetary payments for smoking reduction, efficacy, 1008
motivation for smoking cessation, factor in group program participation, 0209
motor task performance by smokers, effect of stress and personality type, 0530
motor vehicle accidents and moving violations, smoking habit relationship, 1092
neonates, maternal smoking effect, 1312
nicotine and cotinine levels, relationship, 1049
nicotine preference following deprivation or satiation, 0737
noise reactivity, effect of mental and physical stress vs. smoking, 0486
Normative Aging Study in middle-aged men, longitudinal effects, 1046
North Dakota telephone risk factor prevalence survey, 1338
partner-support training for smoking cessation, with/without nicotine gum, comparison, 0707
paternal, effect on son's drug use, 1245
peer group affiliation in adolescents, perceived value as factor in smoking initiation, 1112
pharmacologic effects of various types of nicotine administration, 1012
pharmacological and behavioral factors in withdrawal symptoms, 1118
pharmacological and behavioral variables in smokers, 0992
physician's advice vs. behavior modification vs. self-help methods for cessation, 0121
physician's antismoking intervention, patient's age, sex, and health status as factors, 1084
positive vs. negative approaches to discourage smoking in hospitals, efficacy, 0967
predictive factors at age 19 for smoking at age 31 in males, 0494
pregnant adolescents, prenatal care effect on health behavior during and after delivery, 0658
pregnant women, lifestyle effects on outcome, 0077
pregnant women under age 18, stress and coping as factors in outcome, 0652
prevention of smoking curriculum, efficacy of maximum vs. minimum teacher support, 1235
psychiatric patients, motivational factors in tobacco use, 0098
psychological and physiological smoking cessation program utilizing nicotine chewing gum, 1099
psychological characteristics of heavy smokers, responses to microsocial environment, 0501
psychological factors and group membership influence on smoking habits, 0562
psychophysiological and psychological correlates of nicotine-seeking behavior, 0694
rapid information processing, smoking effect on visual evoked potentials, 0482
recidivism prevention program, behavior conditioning vs. nicotine gum, 0703
relapse factors in long-term maintenance of smoking cessation, 1089
reliability of long-term recall in prevention programs, 0661
secondary reinforcers of smoking behavior, salience in maintenance and satisfaction, 0693
secondary school students, effect of transfer from elementary school on smoking habits, 0596
sedative vs. stimulant smokers, perceived stress and arousal as factors, 0561
self control of smoking, relationship to consistent self-management, 1420
self-help models and manuals for smoking cessation, 1435
self-help smoking cessation, factors, 0104
self-report questionnaire, discrimination of smokers, ex-smokers, nonsmokers, 1513
seventh graders, effect of classroom/television smoking prevention program, 0725
smokeless tobacco use by high school students in Arkansas, factors, 0625
smoking pattern changes in brand switchers, 1017
social skills training as coping strategy in cessation of smoking, efficacy, 0794
spectral analysis, behaviorally based assessment measure of smoking, 0852
stress management component of worksite smoking cessation program, efficacy, 1432
stress-related changes in smoking characteristics, 0481
stressful life events, impact on decision to quit smoking, 0807
student nurses and teachers in England, stereotypic view of smokers and nonsmokers, 0559
taped messages for smoking behavior changes, efficacy, 1508
task performance under stress, effect of transdermal nicotine on cigarette craving, 0736
television series promoting positive health behaviors, effect on smoking cessation, 0198
tobacco use in prehistoric people, psychotropic effects, 0085
tone discrimination task, smoking vs. nonsmoking condition effect on performance, 0484

topographic analysis of smoking behavior, laboratory vs. natural environment, 1125
voluntary brand switchers, smoking pattern changes, 1016
withdrawal symptoms, urges to smoke, cessation problems with nicotine chewing gum, 0129
worksite cessation program, modification as factor, 0691

BENZ(*A*)ANTHRACENES
metabolic pathways of carcinogenic activity, 1018
pancreatic cancers in rats, enzymes and 7, 12-dimethylbenz(*a*)anthracene in etiology, 0871

Benzo(*a*)anthracenes *See* **BENZ(*a*)ANTHRACENES**

Benzo(*c*)phenanthrene *See* **AROMATIC HYDROCARBONS**

Benzofluoranthenes *See* **AROMATIC HYDROCARBONS**

Benzo(*ghi*)perylene *See* **AROMATIC HYDROCARBONS**

Benzophenanthrenes *See* **AROMATIC HYDROCARBONS**

BENZO(*A*)PYRENE
(*See also* AROMATIC HYDROCARBONS)
activation and detoxification of polycyclic hydrocarbons in tobacco condensate, 0354
alcohol consumption effects on metabolism in oral tissue microsomes of smokers and hamsters, 1253
alkaline elution profile of cloned hamster tracheal cell line, effects, 1155
arachidonic acid metabolism in human monocytes, effect, 0488
asymmetric interactions between BaP and DNA, 1102
biotransformation in isolated rabbit hepatocytes, 1315
bronchial cancer induction in hamsters, with cigarette smoke, carbon filter effect, 0175
carcinogenic metabolism inhibition by benzo(*e*)pyrene, 0862
commercial cigarettes, rapid, accurate determination procedure, 1447
cytogenetic effects on bone marrow cells in vivo, 0386
diol epoxide adducts in peripheral blood lymphocytes as indicators of lung cancer risk, 0982
DNA binding assay as dosimeter for lung cancer risk, 1227
DNA binding in placenta and BaP metabolism, smoking effect, 0216
DNA binding, structure of adducts formed, 1159
DNA interactions in carcinogenesis, 0984
enzyme activity effects in pancreatic tissue, 0827
epithelial hyperplasia and metaplasia of airways in hamsters, effect with asbestos, 0358
epoxide hydrolase, metabolic effects, 1453
hormones, effect with nicotine on normal and ectopic production, 1064
human oral mucosa epithelial cells, metabolism and reaction with DNA, 0158
immune cell changes in pregnant mice and progeny, 0820
interferon production effects in tissue cultures and mice, 0939
lung cancer etiology in mice, relationship, 0717
lung cancer etiology, role of carcinogen-metabolizing enzymes, 0872
lung metabolism, alcohol consumption effect, 1347
metabolic activation and detoxification by isozymes of cytochrome P-450, 0838
metabolism and DNA-binding of (^{3}H)benzo(*a*)pyrene to mouse skin, 1212
metabolism by pulmonary alveolar macrophages in baboons, chronic vs. novice smokers, 1467
metabolism rates vs. 7H-dibenzo(*c, g*)carbazole, 1361
metabolites, binding to DNA in mutagenesis, 1449
monoclonal antibodies for quantitation in hemoglobin, 1230
mutagenic activity in rats, tobacco pyrolysates and alcohol consumption effects in rat lung, 1293
nitration effect on biological activity, 1158
nucleic acids, conformational features following carcinogenic modification, 1174
radiolabeled binding, individual response in cigarette smokers as factor in carcinogenesis, 0042
respiratory cancer induction in hamsters, vitamin A effect, 0396
riboflavin, chlorophyllin, chlorophyll, antimutagenic activity, 0394

Benzo(*a*)pyrene hydroxylase *See* **ARYL HYDROCARBON HYDROXYL**

Berylliosis *See* **PNEUMOCONIOSIS**

Betel nut *See* **ARECA**

BIDI SMOKE
mutagenic and carcinogenic compounds, 0266

BIDI SMOKING
industrial workers, risk factor for cancer, 0270
lung cancer etiology in Bangladesh, effect, 0051
mortality rates vs. rates for other forms of tobacco use, 0289
mortality risk factor determination, 0290
pharyngeal and laryngeal cancer risk in males in India, 0271
pulmonary heart disease risk factor with occupation and environment, 0275

Bills *See* **LEGISLATION**

BIOASSAY
animal model for study of Legionnaire's disease, 1497
benzo(*a*)pyrene biotransformation in isolated rabbit hepatocytes, 1315
benzo(*a*)pyrene diolepoxide-DNA adducts in exposed workers, cancer risk detection, 0982
benzo(*a*)pyrene-DNA binding, role in cancer epidemiology, 1227
bronchoalveolar lavage fluid analysis in disease detection, efficacy, 0428
cadmium effects on immune responses of mice, in vivo and in vitro assays, 0687
carcinogen metabolism in liver and pancreatic cells of humans, rats, and hamsters, 1163
carcinogenic mechanisms of metals in tissue culture, 1483
carcinogenicity screening systems for metals, 1258
cigarette smoke condensate mutagenicity, comparison of three assays, 1522
nicotine carcinogenicity of bright vs. burley tobacco, 1218

SUBJECT INDEX

nitrosamines, carcinogenesis testing in animal species, 1199
nitrosation potential of inhaled cigarette smoke in mice, rats, hamsters, 1208
organic chemicals in tobacco leaf, 1034
tissue cultures exposed to mainstream and sidestream smoke, interferon production effects, 0939

BIRTH DEFECTS
congenital heart disease, environmental risk factors including maternal smoking, 1025
maternal drug abuse and smoking relationship, 1043

Birth height *See* **FETAL GROWTH**

BIRTH WEIGHT
(*See also* BODY WEIGHT; FETAL GROWTH; NEONATE; PREMATURITY)
cadmium and zinc interaction in smokers vs. nonsmokers, effect, 1345
cotinine-assisted smoking intervention program, effect, 0969
genetically controlled responsiveness to hydrocarbons, effect with cigarette smoke in mice, 0212
hemoglobin levels in women who smoke during pregnancy, relationship, 0415
infants of mothers in community reproductive care program, factors, 0077
maternal alcohol consumption and smoking, effects, 0117
maternal smoking and other risk factors, 0360
maternal smoking effect, 0045
maternal smoking effects at high altitudes, 0755
prenatal care and smoking as factors, blacks vs. whites in Kansas City, 1141
ureaplasmas, colonization in placenta, effect with maternal smoking, 1051

BLADDER
(*See also* UROGENITAL SYSTEM)
papillomas, smoking relationship to malignant changes, 1026

BLADDER NEOPLASMS
(*See also* UROGENITAL NEOPLASMS)
catechol effect on development in rats treated with N-butyl-N-(4-hydroxybutyl)nitrosamine, 1210
cigar and pipe smokers, risk relationship, 1009
cigarette smokers, risk relationship of type of exposure, 1010
diet as risk factor with alcohol consumption and smoking, long-term study, 1275
epidemiology, risk factor determination, 0091
etiology, tobacco and other environmental factors, 0858
mortality, bronchial cancer as secondary cause, smoking effect, 0540
papillomas to cancer, smoking relationship, 1026
residents of rural areas, tobacco consumption as risk factor, 0164

BLOOD
(*See also* ERYTHROCYTES, LEUKOCYTES)
alpha 1-protease inhibitor concentration, smokers vs. nonsmokers, 0906
aneurysm patients, antiproteolytic capacity in smokers, 0630
antibodies as markers for early detection of lung cancer, 0116
carboxyhemoglobin levels in blood bank samples, toxic risk, smoking relationship, 1152
catecholamine concentrations in plasma of rabbits, intravenous nicotine effects, 1021
chronic airflow limitation relationship to vitamin C levels in smokers vs. nonsmokers, 0125
cigarette smoke vs. methylamine vs. buffer, effect on hemolytic activity, 1281
dosimetry of 4-aminobiphenyl using blood protein adducts, 1077
elastase activity of human peripheral blood monocytes, emphysema relationship, 1475
elastase and trypsin inhibiting capacity, smoking effect, 0110
elastase levels in smokers before/after acute smoking, vs. nonsmokers, 0113
estradiol levels in infertile men, smoking effect, 1098
gingival vascular response to plaque accumulation in smokers vs. nonsmokers, 0455
granulocyte count relationship to bone marrow production in smoke-exposed mice, 0886
heat-stable alkaline phosphatase as tumor marker in nonsmokers, 0636
hemoglobin—oxygen affinity and carboxyhemoglobin level correlation, smoking effect, 0439
immunoglobulin D in smokers vs. ex-smokers vs. nonsmokers, 0963
immunoglobulin E, patterns in cigarette smokers vs. ex-smokers, 0958
leukocyte, neutrophil, and lymphocyte concentration in smokers vs. nonsmokers, 0220
lipoprotein composition and metabolism in monkeys, oral nicotine administration effects, 1082
nicotine added to platelet-rich plasma, coagulation and aggregation effects vs. smoking, 0230
nicotine and cotinine levels in brand switchers, changes over study period, 1017
nicotine effect on volume changes in main and digital vessels, 0842
nicotine effects on leukocytes and platelets at molecular level, 1285
nicotine levels before and after smoking in patients with renal failure, 1438
nicotine levels in pregnant ewes, chronic exposure effects, 0671
N-nitrosamines, determination, 1404
physiological and biochemical parameters in smokers vs. nonsmokers, 0436
plasma before and after smoking, effect on cultured mesothelial cells, 0536
plasma fibrinogen levels in smokers, cardiovascular disease relationship, 0541
platelet activating factor levels in smokers vs. nonsmokers, 0047
platelet behavior, fibrinolysis, and hemorrheology in habitual smokers, 0586
red blood cells, antioxidant variations in smokers, 0759
retinol, beta-carotene, vitamin E, selenium levels, smoking relationship, 1001
serum antibody to *Micropolyspora faeni* in farmers, smokers vs. nonsmokers, 0366
serum protein composition, protein binding of drugs, smoking effect, 0899

SUBJECT INDEX

sister chromatid exchanges in workers exposed to phenoxy acid herbicides, smoking effect, 0196
thiocyanate level, confirmation of self-reported smoking behavior in prevention trial, 0057
thiocyanate levels in umbilical cord, maternal smoking effect, 0423
white blood cell metabolism, changes caused by smoke components, 0183
white cell count, ischemic heart disease relationship, with smoking, 0598

BLOOD CHEMICAL ANALYSIS
cadmium levels in smokers and nonsmokers, 1298
carboxyhemoglobin, thiocyanates, nicotine, cotinine levels, smoking behavior relationship, 0905
cotinine levels in pregnant women, measurement to encourage smoking reduction, efficacy, 0969
cotinine levels in smokers who switch from high- to low-tar cigarettes, 0533
6-keto PGF$_{1}\alpha$ and thromboxane B_2 in healthy volunteers, smoking effect, 0377
lead and cadmium levels in copper smelter workers, smoking effect, 1244
melatonin, alkaline phosphatase levels in elderly, smoking effect, 0218
nicotine and cotinine levels in smokers who switch to low-yield brands, 1215
nicotine, cotinine, thiocyanate, and other components as indicators of oral cancer risk, 1184
nicotine, cotinine, thiocyanates, hydroxyproline levels in smokers vs. nonsmokers, 0375
urea nitrogen, creatinine, and nicotine before and after smoking and hemodialysis, 1437
zinc levels in maternal and cord blood, exposure effects in smokers vs. nonsmokers, 1345

BLOOD CHOLESTEROL
(*See also* HYPERCHOLESTEREMIA; LIPIDS)
cancer mortality in middle-aged men, risk factor with smoking, 1128
cardiovascular disease morbidity and mortality, risk factor with smoking, 0814
cessation of smoking effect on high and low density lipoprotein cholesterol, 0119
coronary bypass patients, diet and drug treatment program effects, smoking relationship, 0719
coronary disease risk factor, 10-year followup of intervention trial in Sweden, 0473
coronary heart disease, risk factor with smoking, 0414
exercise, alcohol consumption, and smoking effects in premenopausal women, 0934
exercise level and smoking effects, 0942
high and low density in air crewmen, coronary disease risk determinant, 1465
low and high density lipoproteins, cardiovascular disease risk relationship, smoking factor, 0700
middle-aged male myocardial infarct patients, rehabilitation program effect, 0399
middle-aged men, coronary disease mortality risk factor, 0676
middle-aged men in Sweden, heart disease and cancer risk relationship, with smoking, 0474
Normative Aging Study in middle-aged men, risk factor for coronary disease, 1046
tobacco chewers and cigarette smokers, dose—response effect, 0285
women, relationship to coronary disease in smokers, Framingham study participants, 0987

BLOOD CIRCULATION
(*See also* HEART FUNCTION; HEMODYNAMICS; ISCHEMIA)
arterial and capillary flow in skin, cigarette nicotine content effect, 0914
cessation of smoking effect on cerebral gray matter blood flow, 1486
coronary disease patients, smoking effect, 0887
cutaneous blood flow in arteriosclerosis, 0955
diabetics, smoking as factor, 0139
duodenal mucosal blood flow, cigarette smoke and i.v. nicotine effects in rats, 0748
fetal, nicotine effect on amino acid transport, 1456
intestinal flow in dogs, nicotine effect, 1357
nicotine effect in canine stomach, 1358
nicotine effect on flow and embryo development in rats, 1111
nicotine effect relative to myocardial oxygen demand, 1408
patency of saphenous vein vs. e-PTEE grafts, 0742
pregnant ewes, chronic smoke exposure effects, 0671
sarcoidosis patients, impairment in lungs of smokers, 0094
smoke inhalation effects in brain of bullfrogs, 0364
vertebral flow in dogs, effect of nicotine lactate, 1500

BLOOD COAGULATION
coronary arteries, smoking effect, 1554
hypercoagulability following acute smoking, 0586

BLOOD LIPIDS
cessation of smoking effect, 0119

BLOOD PLATELETS
adherence to rabbit aorta, smokers of medium-tar cigarettes, 0535
adhesion to endothelial surface, before and after smoking, 0538
aggregability, smoking effect on thromboxane A_2 and prostacyclin production, 1458
aggregation, acute smoking effects, 0586
aggregation by tumor cells and adhesion to endothelium, nicotine interactions, 0613
arachidonic acid metabolism, effect of smoking and nicotine, 0612
carbon monoxide inhibition of aggregation and release function, 0623
chronic exposure to smoke in rats, effects, 0890
hydroxyethylrutosides effect on smoking-induced changes in aggregate ratio, 1146
myocardial infarct patients, influence of smoking, diabetes, sex on aggregation, 0608
nicotine effects at molecular level, 1285
nicotine effects, cigarette level as factor, 0230
nicotine effects on function and catecholamine release, 0738
saturated fat intake and smoking in Scottish farmers, effects, 0229
thrombosis and clotting, cigarette smoke effects, 1554
thromboxane and prostaglandin synthesis, nicotine effects, 0452

thromboxane production following acute and chronic tobacco exposure, 0047

BLOOD PRESSURE
adolescents, negative relationship with smoking, 0305
arterial regulation in rats, smoke inhalation effect, 0904
cadmium and lead in urine, correlation, smoking effect, 0056
cadmium and zinc intake in smokers, relationship, 1236
cardiovascular disease mortality, risk factor with smoking, 0814
cessation of smoking effect, 0119
coronary disease risk factor, 10-year followup of intervention trial in Sweden, 0473
diabetic vs. healthy smokers, 0141
fetus, maternal smoking effect in baboons, 1231
health education for cardiovascular risk reduction in children and parents, 1411
hypertension, factors in etiology, 1444
Japanese men born and living in Hawaii, coronary disease risk factor with smoking, 0828
low penile pressure in males with erectile dysfunction, arterial disease risk, 0765
maternal smoking effects in mother and fetus, 0192
middle-aged men, coronary disease mortality risk factor, 0676
middle-aged men in Sweden, heart disease and cancer mortality risk, with smoking, 0474
nicotine and cigarette smoke effects in monkeys and cats, 0264
nicotine effect, 0210
normotensive vs. hypertensive subjects, smoking effect, 1224
smoke inhalation effects in brain of bullfrogs, 0364
stress manifestation, alcohol consumption and smoking as modifiers, 1265
Vitamin C and acute smoking effects, 0604

Blood pressure, high *See* **HYPERTENSION**

BLOOD SUGAR
cessation of smoking effect, 0119

BLOOD VESSELS
(*See also* CARDIOVASCULAR SYSTEM; ARTERIES)
antidotic substances in pine oleoresin to counteract effects of tobacco smoke, 0369
arachidonic acid metabolism in endothelium, effect of smoking and nicotine, 0612
coronary vascular reactivity changes following cadmium exposure in rats, 0912
diabetics, microcirculation in smokers vs. nonsmokers, 0140
dilator and constrictor responses in gray matter of smokers vs. nonsmokers, 1484
fetal, pulse wave volume and maternal smoking effects, 0469
fibrinolytic activity of vein walls, effect of oral contraceptives and smoking, 0450
main and digital, nicotine effect on blood volume changes, 0842
oral contraceptive use and smoking effects on prostacyclin activity in smooth muscle cells, 0321
pinocystolic activity in smokers vs. nonsmokers, 0170
prostacyclin and fibronectin production in umbilical vein cells of smokers vs. nonsmokers, 0322
saphenous vein vs. e-PTEE grafts in bypass procedures, 0742
umbilical veins, inhibitory effect of nicotine on amino acid uptake, 1455

BODY TEMPERATURE
nicotine effects in C3H and C57BL mice, 0763

BODY WEIGHT
(*See also* BIRTH WEIGHT, OBESITY)
cessation of smoking, behavioral factors and biological mechanisms of change, 1020
cessation of smoking by women in Sweden, relationship, 0464
cessation of smoking effect, 0119
coronary disease risk relationship with educational level, 0297
dietary vitamin C intake effect in smoke-exposed hamsters, 0367
lipoprotein lipase activity as factor in overweight dieting smokers vs. nonsmokers, 0762
oral leukoplakia risk relationship, 1459
renal cell carcinoma risk factor, 1363

BONE
marrow production of inflammatory cells and precursor stem cells, smoking effect in mice, 0886
mineral loss in smokers vs. nonsmokers, 0261

BONE DISEASES
degenerative changes in intervertebral discs in rats, risk factor, 1500
osteoporosis and fractures in smokers vs. nonsmokers, 0261

Bradycardia *See* **ARRYTHMIA**

BRAIN
(*See also* CENTRAL NERVOUS SYSTEM)
blood pressure and circulation effects of smoke inhalation in bullfrogs, 0364
carotid artery atherosclerosis, smoking effect, 1115
cortical slow potentials, smoking effect under stressful and nonstressful conditions, 0530
electroencephalographic abnormalities during long-term withdrawal from smoking, 0324
fetal, carbon monoxide exposure effect on neurochemical development, 1003
hippocampus and reticular formation, nicotine sites of action in rats, 1514
neuropeptide secretion in mice, nicotine effects, 0763
nicotine and serotonin receptors in humans, smoking effects, 0584
nicotine binding sites in mice, effect of endogenous brain material, 1252
nicotine binding sites in rat brain and central nervous system, 0910
nicotine effects in rats, 0521
nicotine receptors in rat brain, isolation and characterization, 1286
nicotine tolerance, genetic factors and role of nicotinic receptors, 0757
nicotinic ligand binding, central nervous system effects, 0520
psychopharmacology of nicotine sulfate in rats with nucleus basalis magnocellularis lesions, 1562
rapid information processing, smoking effect on visual evoked potentials, 0482

SUBJECT INDEX

right vs. left cerebral hemisphere activity in abstinent smokers, 0744

BRAIN NEOPLASMS
central nervous system tumors, environmental and occupational exposures as factors, 1478
children and adolescents, passive smoking as factor, 0733
gliomas in infants, passive smoking as factor in etiology, 1256

BREAST FEEDING
attitudes during pregnancy, effect with smoking 6 and 12 months postpartum, 0041
infant morbidity, effect compared to formula-fed, maternal factors, 0878

Breast neoplasms *See* MAMMARY NEOPLASMS

BRONCHI
(*See also* BRONCHIOLES; LUNGS)
activation/deactivation of cigarette smoke mutagens by homogenized tissue, 0337
airspace size ranges in smokers vs. nonsmokers, 1260
airway response to methacholine in nonsmokers, asymptomatic smokers, symptomatic smokers, 0277
alpha$_1$-protease inhibitor activity in bronchoalveolar lavage fluid, smoking effect, 0115
alveolar lavage tests in respiratory disease patients, smokers vs. nonsmokers, 0378
atypia in soot and BCME exposed workers, smoking as factor, 0444
elastase activity in bronchoalveolar lavage fluid, smoking effect, 0111
goblet cell density in patients with bronchitis vs. smokers vs. nonsmokers, 0160
histamine and leukotriene levels, smoking effect, 0181
histamine responsiveness as early indicator of airflow obstruction, 0043
hyperreactivity, induction mechanism in guinea pigs, 0108
methacholine response before and after smoking two cigarettes, 0391
phospholipids in bronchoalveolar lavage, smokers vs. nonsmokers, 0544
radon decay products on smoke tar particles, selective deposition, 0752
washings vs. mucosal specimens, values and limits for bacteriological study, 0426

BRONCHIAL DISEASES
(*See also* ASTHMA; BRONCHITIS; CHRONIC BRONCHOPULMONARY DISEASE; OBSTRUCTIVE AIRWAY DISEASES; RESPIRATORY TRACT DISEASES)
bronchoalveolar lavage in diagnosis and disease progression, 0428
obstructive bronchitis, smoking relationship, 0182
pulmonary fibrosis, etiologic agents determination, 1498
rheological properties in sputum of chronic bronchitics, smokers vs. nonsmokers, 0323
syptoms suggestive of asthma in snow crab processing workers, smoking as factor, 0084

BRONCHIAL EPITHELIUM
B_{12} and folate deficiency in neoplastic transformation, 0606
carcinogens in sidestream smoke, inhibition of localization, 0935
changing patterns of damage in long-term smoke-exposed dogs, 1178
cytopathological, cytochemical, and prospective studies of abnormalities in smokers, 0462
histologic changes related to reduced tar and nicotine cigarettes, 1177
permeability in smokers vs. nonsmokers, 0651
preneoplastic cell markers in sputum for early diagnosis, 1461
squamous metaplasia in smoke-exposed dogs, 1180
structure and cell replacement rates in nonsmokers, ex-smokers, and smokers, 0575

BRONCHIAL MUCOSA
biopsy specimens, value for bacteriological study vs. bronchial washings, 0426
epithelial cell structure and replacement rate, smokers vs. ex-smokers vs. nonsmokers, 0575

BRONCHIAL NEOPLASMS
chemoprevention in patients with asbestos-related lung diseases, 1531
gas and particulate phases of cigarette smoke in induction in hamsters, carbon filter effect, 0175
secondary cause of death in bladder cancer patients, smoking effect, 0540
uranium miners exposed to radon-222, risk with smoking, 0097

Bronchiectasis *See* BRONCHIAL DISEASES

BRONCHIOLES
(*See also* BRONCHI)
analysis for determining etiology of pulmonary fibrosis, 1498
high-rate diet and smoke effects on lung tissue morphology in monkeys, 0868

BRONCHITIS
(*See also* BRONCHIAL DISEASES)

bacterial adherence in colonization of airways of patients, smokers vs. nonsmokers, 1249
cell populations in bronchoalveolar lavage fluid, relationship, 1538
cessation of smoking in patients, method as factor, 0191
diurnal variations in airway obstruction in patients, smoking effect, 0512
goblet cell density in patients vs. smokers vs. nonsmokers, 0160
infancy and childhood, long-term effect with smoking on lung function, 0044
males over age 55, smokers vs. nonsmokers, 0279
mortality in cadmium-exposed workers, 0529
pulmonary clearance in smoking vs. ex-smoking patients, 0550
pulmonary function adaptation to ozone in smokers with chronic bronchitis, 1024
questionnaires as screening instruments for asbestos workers, 0460
reverse chutta smokers in India, length of habit as factor, 0281
rheological properties of bronchial fluids, smokers vs. nonsmokers, 0323
urban vs. rural residence, factor with smoking on incidence, 0427
Vitamin A intake in milk as protection, smoking as factor, 1007

SUBJECT INDEX

Bronchogenic carcinoma *See* **CARCINOMA, BRONCHOGENIC**

Buccal cancer *See* **MOUTH NEOPLASMS**

Buergers disease *See* **THROMBOANGIITIS OBLITERANS**

Byssinosis *See* **PNEUMOCONIOSIS**

CADMIUM
  absorption in smokers, effect on nutritional intake of zinc, 1236
  accumulation mechanism in tobacco, 0923
  biological implications of tobacco content, 0751
  blood and urine levels in copper smelter workers, smoking effect, 1244
  coronary vascular reactivity changes following exposure in rats, 0912
  environmental and industrial exposure, synergistic effect of smoking on body burden, 1221
  epithelial type II cells, sensitivity, 1121
  gastrointestinal processes, effects with nicotine, 0628
  immune system, in vivo and in vitro effects, 0687
  liver and kidney levels in smokers and nonsmokers, 1298
  metallic elements, carcinogenicity screening systems, 1258
  mortality in exposed workers, 0529
  placental pharmacokinetics, 1288
  serum levels in cab drivers, respiratory disease relationship, 0241
  soil and leaf levels on Ontario farms, 0062
  teratogenic effect of chronic exposure in pregnant hamsters, 1164
  tobacco grown on sludge-amended soil, levels, 1030
  tobacco leaf and root content, potential reduction, 0916
  urinary levels in population with low exposure, smoking effect, 0056
  zinc levels in maternal and cord blood, exposure effects in smokers vs. nonsmokers, 1345

Cancer *See* **NEOPLASMS**

CANNABIS
  (*See also* DRUG ABUSE)
  chemical/biological analysis of smoke condensate, 1320

Capillaries *See* **BLOOD VESSELS**

CARBAZOLES
  (*See also* HETEROCYCLIC NITROGEN COMPOUNDS)
  metabolism and mechanism of action of 7H-dibenzo(*c, g*)carbazole, 1361

CARBOHYDRATE CONTENT
  chewing tobacco, dental and periodontal disease relationship, 1405
  chutta tobacco from southeast India, 0278
  near infrared spectroscopy of tobacco and tobacco products, 1318

CARBOHYDRATES
  plant carbon and nitrogen content effects, 0921

CARBON DIOXIDE
  carbon and nitrogen pools interrelationship, 0921

CARBON MONOXIDE
  arterial wall hypoxia induction, effect on arteriosclerosis etiology, 0839
  atherogenic effect in hamsters, 1203
  Biofeedback Smoking Education Program, expired air levels as feedback element, 0835
  blood levels as smoking status determinant, 0215
  carbon monoxidase for detection and conversion in tobacco smoke, 1303
  cardiomyopathy effects in rabbits, 0155
  cardiovascular effects in rats, at ambient and high altitudes, 1469
  cigarette structural alterations to reduce yield, 0928
  coronary artery disease patients, acute effects of exposure in nonsmokers, 0649
  endurance time for physical activity, effects vs. smoke inhalation, 0169
  exhalation levels in smokers, nonsmokers, and smokers who are quitting, 1400
  expired air levels in brand switchers, changes over study period, 1017
  expired air levels, knowledge by patients as tool for smoking cessation, efficacy, 0548
  expired air of children aged 10 and 11 as indicator of passive smoke exposure, 0569
  feedback information in cessation program, efficacy at 6, 12, 18 months postclinic, 0786
  gestational exposure effects on brain neurochemical development, 1003
  monitoring smoking reduction, efficacy, 1008
  neuroendocrine effects in humans, 0746
  occupational exposure as factor in poisoning, with smoking, 0440
  pollutant levels in smoking-restricted vs. smoking-permitted buildings, 0100
  portable, low-cost, reliable measuring devices for validation of survey data, 0588
  prostacyclin production in the heart, effect with nicotine, 0738
  tidal air boosts in deprived inhalers vs. noninhalers, 0487

CARBON MONOXIDE CONTENT
  (*See also* CARBOXYHEMOGLOBIN LEVELS)
  British cigarettes, changing levels, 0527
  cigarette preference relationship, with sweet-bitter taste dimension, 0795
  cigarettes rated by Federal Trade Commission, testing apparatus, 0777
  domestic and imported cigarettes in Australia, 0007
  Italian cigarettes, 0331

CARBOXYHEMOGLOBIN LEVELS
  (*See also* CARBON MONOXIDE CONTENT)
  blood bank samples, smoking effect, 1152
  blood concentrations, cigarette yield, smoking history and behavior as determinants, 0905
  calculated and measured in patients with respiratory disease, smoking effect, 0075
  diabetic women during pregnancy, smokers vs. nonsmokers, 0156
  hemoglobin—oxygen affinity correlation, acute tobacco intoxication effect, 0439

- leukocyte and neutrophil blood concentration correlation, 0220
- passive smokers vs. smokers vs. nonsmokers, 0194
- smoke inhalation model, to discriminate between different cigarettes, 0480
- urinary mutagens, correlation in cigarette vs. sham-smoking baboons, 1467

CARCINOGENESIS
- (*See also* NEOPLASMS)
- analytical studies in tobacco carcinogenesis, assay methods for chemical compounds, 1211
- benzo(*a*)pyrene-DNA binding assay as dosimeter for lung cancer risk, 1227
- benzo(*a*)pyrene, nitration effect on biological activity, 1158
- benzo(*a*)pyrene, P-450 enzyme system in activation, 0354
- biochemical mechanisms of nitrosamine carcinogenesis, 1353
- biomarkers in high-risk asbestos-exposed shipyard workers, 0678
- bladder cancer, smoking and occupational exposure as factors, 0091
- bronchial metaplasia, vitamin B$_{12}$ and folate deficiency in smokers as factor, 0606
- buccal pouch tumors in hamsters, role of vitamin E, 1059
- cerebral tumors, smoking and other factors in etiology, 0093
- cotinine and nicotine-N′ -oxides, effect on tumor development in rats, 1210
- cytochrome P$_1$-450 activity in smokers, effect on susceptibility to cancers, 0848
- cytotoxic cell function in lung cancer etiology, 0964
- esophageal, nitrosamine and catechol in etiology in rats, 1160
- laryngeal cancer, effect of alcohol and smoking, 0296
- lung cancer, air pollution, alcohol consumption, and smoking in etiology, 0187
- lung cancer, progressive epithelial process, detection with sputum cytology, 0462
- lung tumors in mice, role of beta-glucuronidase and inhibitors, 1354
- metabolic activations of 12 monobenz(*a*)anthracenes, 1018
- N-nitrosamine, screening for inhibitors, 1201
- Nebraska Laboratory Cancer Research Center, objectives, 1154
- nicotine bioactivation and metabolism, relationship, 0708
- nicotine levels and tumor incidence in mice, 1238
- nitrosamines at concentrations found in snuff, effect in rats, 0993
- nitrosamines, biochemical pathway of β-oxidized nitrosamines, 1145
- nitrosamines, chemical processes involved in formation and inhibition, 1144
- nitrosamines in animal species, ELISA method, 1199
- nitrosamines, inhibition by alcohols of localization in tumor sites, 0936
- oral cancer, alcohol consumption and smoking in etiology, 0345
- oral lichen planus lesions, mouth cancer relationship with smoking, 0163
- phenotypic analysis of epithelial cell neoplastic progression, 1507
- secretory component of immunoglobulin A as marker of neoplastic growth, smoking effect, 0768
- squamous cell carcinoma of the oral cavity, gamma-glutamyltranspeptidase relationship, 0841
- 3-methylcholanthrene in rat liver, 1156
- tumoricidal potential of pulmonary alveolar macrophages, smoking effect, 0803

CARCINOGENICITY REDUCTION
- dietary antioxidant intake effects on toxicity of tobacco smoke in hamsters, 0367
- protein removal effects, 0603

CARCINOGENS
- (*See also* COCARCINOGENS; MUTAGENS)
- 4-aminobiphenyl, 1077
- benzo(*a*)pyrene, 0158
- cytochrome P-450, epoxide hydrolase, bioactivation and detoxification, 0838
- dihydrodiols of polycyclic aromatic hydrocarbons, metabolic formation, 0190
- DNA adducts, analysis method for detection, 1460
- DNA interactions, immunological investigation, 0984
- environmental, report on analysis methods by International Agency for Research on Cancer, 0250
- gas and particulate phases of cigarette smoke, carbon filtration effects on activity, 0175
- (^{3}H)benzo(*a*)pyrene, catechol effect on metabolism and DNA-binding to mouse skin, 1212
- 7H-dibenzo(*c, g*)carbazole, 1361
- metal compounds, mechanisms in tissue culture, 1483
- metallic elements, carcinogenicity screening systems, 1258
- N-nitrosodimethylamine, potentiating effects of sex hormones in mice, 0781
- Nebraska Laboratory Cancer Research Center, objectives, 1154
- nitrosamines, 0936
- nucleic acids, conformational features following carcinogenic modification, 1174
- occupational exposure and smoking in lung cancer, 0327
- polycyclic aromatic hydrocarbons, structure—activity relationships and relative carcinogenicity, 1365
- sensitivity differences, cytochrome P-450 identification and phenotyping in determination, 0990
- sidestream smoke components, inhibition of localization in epithelial tissues, 0935
- tobacco and tobacco smoke components, carcinogenesis study methods, 1207
- tobacco flavor compounds in low-tar cigarettes, 1198
- tobacco-related, alcohol consumption effect on metabolism, 1347
- tobacco-specific, induction by beta-glucuronidase in mice, 1354
- 12 monobenz(*a*)anthracenes, differences in metabolic activation, 1018

CARCINOMA, BRONCHOGENIC
- (*See also* BRONCHIAL NEOPLASMS; LUNG NEOPLASMS)
- levels of IgA and secretory components in patients, 1333
- nonspecific airway reactivity in patients, smoking relationship, 0101
- screening and treatment of high-risk men, effectiveness, 1241

CARCINOMA, EPIDERMOID
- (*See also* BRONCHIAL NEOPLASMS; LUNG NEOPLASMS; SKIN NEOPLASMS)
- cytomorphological criteria for early detection in smokers, 0462
- males and females in Shanghai, smoking-related risk for lung cancer, 0142

physical examination to determine high risk profile, 1459
reverse smoking and smoking relationship in Colombia, 0150
women in Japan, smoking as risk factor, 0355

Cardiac *See* **HEART**

CARDIOVASCULAR DISEASES
(*See also* HEART DISEASES, VASCULAR DISEASES)
alcohol consumption and smoking, risk relationship, 0700
atherosclerosis in patients with renal failure, factors, 1534
cessation of smoking effect on risk factors, 0119
family diagnosis and therapy, comparison of treatment approaches, 1356
Framingham Offspring Study, Cycle III, 1041
health education for children and parents for risk reduction, 1411
hemostatic variables in pathogenesis, smoking relationship, 0541
Hispanic children to age 18 in Texas, risk factor study, 1464
Kaunas-Rotterdam Intervention Study, 0397
lifetime tobacco consumption correlation with incidence, 1037
Minnesota Heart Health Program for reduction through community education, 1120
MONICA project, trends and determinants of mortality/morbidity, 0059
mortality, smoking relationship, 0472
Normative Aging Study in middle-aged men, longitudinal effects, 1046
North Karelia intervention program, effect on smoking habits, 0197
nurses, smoking and other risk factors, long-term followup, 1054
peripheral arterial disease in risk prediction, 0699
physical activity as protection, smoking relationship, 0718
physical fitness, relationship with smoking and other risk factors in men, 0078
prostacyclin and thromboxane production in chronic smokers, relationship, 0668
prostacyclin synthetase inhibition by nicotine in etiology, 0500
red blood cell antioxidants, variations in smokers, relationship, 0759
risk factor assessment, 0016
small town population in New Zealand, fourth risk factor survey, 0405
stroke, population-based study of long-term predictors, smoking as risk factor, 0698
stroke, risk factors in Japanese men born and living in Hawaii, 0828
survey of risk factors in middle-age persons in Scotland, 0582
women, prospective study of risk factors, 1078

CARDIOVASCULAR SYSTEM
(*See also* BLOOD VESSELS, HEART)
antidotic substances in pine oleoresin to counteract effects of tobacco smoke, 0369
arterial blood pressure regulation, effect of chronic smoke exposure in rats, 0904
arteriovenous fistulas used in renal dialysis, smoking effect on long-term patency, 0595
aversive smoking cessation program, effect on cardiac response, 1553
biochemical and physiological effects of niotine-related substances, 0370
blood carboxyhemoglobin levels from smoking and air pollution, risk, 1152
carbon monoxide exposure at ambient and high altitude in rats, effects, 1469
exercise response before and after beta adrenoceptor blockade, smokers vs nonsmokers, 0601
experimental smoking conditions, responses in humans and rabbits, 0371
fibrinolytic activity of vein walls, effect of oral contraceptives and smoking, 0450
Framingham Offspring Study, Cycle III, 1041
high- and low-nicotine cigarettes and nicotine gum, comparative effects, 0681
low- vs high- nicotine cigarettes, effect on prostacyclin and thromboxane balance, 0668
maternal and fetal response to smoking, 0449
nicotine and cigarette smoke effects in monkeys and cats, 0264
nicotine effect on main and digital vessels, 0842
Normative Aging Study in middle-aged men, longitudinal effects, 1046
pinocystolic activity in smokers vs. nonsmokers, 0170
small blood vessels in diabetic patients, changes in smokers vs. nonsmokers, 0139
smoking effects, measurement, 0380
surgery patients who smoke, presurgery abstinence effect, 0513
vascular prostanoid synthesis, effect of plasma from smokers, 0047
vasoconstricting effect of nicotine on fetal growth in women who smoke, 0379
vasodilator and vasoconstrictor responses in gray matter of smokers vs. nonsmokers, 1484

Catechol *See* **PHENOLS**

CATECHOLAMINES
(*See also* ADRENAL HORMONES)
cortical release of ^{3}H-noradrenaline in rats, nicotine administration effect, 1511
dopamine activity in rat brain tissue, acute and chronic nicotine administration, effects, 0941
dopamine and noradrenaline levels in rats, smoke exposure effects, 0454
metabolism in mouse brain, nicotine effect, 0763
nicotine effect on release in blood platelets, 0738
normotensive vs. hypertensive subjects, smoking effect, 1224
plasma concentrations in rabbits, intravenous nicotine effects, 1021
platelet aggregation before and after smoking, saturated fat intake as factor, 0229
pregnant ewes, effect of smoke exposure on release, 0671
synthesis and release, nicotine effect, 1479

CELLS
(*See also* ERYTHROCYTES, LEUKOCYTES)
atypical in bronchi of soot and BCME exposed workers, smoking as factor, 0444
benzo(*a*)pyrene, cytogenetic effects on bone marrow cells in vivo, 0386

C5 role in initiating inflammatory cells influx in lung disease etiology, 0753
carcinogen metabolism in liver, pancreatic acinar, and pancreatic duct cells, 1163
cell wall and soluble cell fractions, particulates contribution, 0922
cultured umbilical vein, prostacyclin and fibronectin production in smokers vs. nonsmokers, 0322
cytolytic functions of pulmonary effector cells, smoke inhalation effects in mice, 0903
endothelial, hydroxyethylrutosides effect on smoking-induced changes, 1146
endothelial, platelet adhesion before and after smoking, 0538
exocrine pancreas, effect of 7, 12-dimethylbenz(*a*)anthracene, 0871
glycoprotein and polypeptide biosynthesis in murine cells exposed to sidestream smoke, 0937
goblet cell density in bronchitics vs. smokers vs. nonsmokers, 0160
hamster embryo, cocarcinogenic effects of tobacco with known environmental carcinogens, 0412
intracellular spicules in smoke-exposed rat lung, ultrastructure and distribution, 1343
lung cancer cells incubated with cigarette smoke, DNA strand breaks, 0385
melanin in pigmented gingival tissue of smokers and nonsmokers, 0461
mesothelial, cigarette smoke induced cytotoxicity, 0536
nicotine and benzo(*a*)pyrene, effect on hormone production and cellular DNA, 1064
nicotine and human endothelium-platelet-tumor cell interactions, 0613
nicotine uptake, acetylcholine receptors and cell membrane permeability, 1479
pinocystolic activity in endothelial cells of smokers vs. nonsmokers, 0170
pulmonary, cellular and subcellular effects in offspring of smoke-exposed rats, 0778
red blood cells deformability, acute tobacco intoxication effect, 0439
smooth muscle cells, physiological effects of nicotine, 1093
T, B, macrophages in pregnant mice and progeny, effects of benzo(*a*)pyrene, 0820
T cells in rats, smoke exposure effects on immune response, 0915
ultrastructure of rat thoracic aorta, nicotine effects, 0537

CELLS, EPITHELIAL
atypical bronchial epithelial cells in sputum as markers of people at risk for lung cancer, 1461
benzo(*a*)pyrene metabolism in oral mucosa, 0158
cadmium, sensitivity of type II cells, 1121
enzymes in bronchiolar cells, carcinogen-metabolizing activity in lung cancer etiology, 0872
gingiva permeability to nitrosonornicotine, 0875
hyperplasia and metaplasia in hamsters, effect of asbestos and benzo(*a*)pyrene, 0358
keto oleic acids as inflammagens, 1309
lungs, secretory component as indicator of dysfunction, smoking effect, 0768
nitrogen dioxide and ozone, long-term effects in monkeys, 0653
permeability in smoke- and elastase/smoke-exposed hamsters, 1119
permeability of respiratory epithelium in smokers vs. nonsmokers, 0651
phenotypic analysis of epithelial cell neoplastic progression, 1507
respiratory, smoke-induced inflammation in guinea pigs, mechanisms, 0108
sidestream smoke carcinogens, inhibition of localization in epithelial tissues, 0935
structure and replacement rate in bronchi of smokers, ex-smokers, nonsmokers, 0575

CENTRAL NERVOUS SYSTEM
(*See also* BRAIN)
nicotine and acetylcholine high-affinity binding, autoradiographic mapping, 0983
nicotine and nicotinic agonists binding in brain tissue, effects, 0520
nicotine binding sites, and in rat brain, 0910
nicotine, effect in primates, 0817
nicotine effects, 1107
nicotine influence on neuronal expression of acetylcholine receptors, 0616
opioid peptides, regulation of oxytocin and vasopressing, nicotine effect, 1392
primary tumors, environmental and occupational exposures as factors, 1478
snuff-dipping and tobacco chewing, effects, 1463

CEREBROVASCULAR CIRCULATION
(*See also* BLOOD CIRCULATION)
vasodilator and vasoconstrictor responses in smokers vs. nonsmokers, 1484

CEREBROVASCULAR DISORDERS
(*See also* VASCULAR DISEASES)
blood flow reduction in smokers, risk relationship, 1487
cessation of smoking effect on risk, 1486
hypertensive patients, risk factors with smoking, 1485
MONICA project, West Germany, monitoring of trends and determinants, 0176
stroke, risk in chronic cigarette smokers, 1484
tumor etiology, smoking and other factors, 0093

CESSATION OF SMOKING
(*See also* RECIDIVISM REDUCTION OF SMOKING: WITHDRAWAL CLINICS)
addicted vs. environmentally influenced smokers, effect of treatment type, 0866
adolescent personality dimensions, predictors of ability to quit as adult, 0674
adolescents, effect of health education assemblies, 1042
adolescents in manual and technical trade schools, health education program component, 0478
adolescents, respiratory function tests as tool in education program, 0330
adult Americans, measure of health strategies and behaviors, 1396
angina patients in minimum-contact intervention program, 1496
armed forces in Egypt, efficacy of various program components, 0173
attitudes associated with maintaining abstinence, 0525

SUBJECT INDEX

attitudes of university hospital staff, faculty, and students, 0207
California physicians, cancer mortality, 0685
Cancer Information Service, telephone communication network for smokers who want to quit, 1307
cardiovascular disease risk reduction, 0168
causal attributions for abstinence, nonabstinence, lapse, and relapse, 1368
cerebrovascular disease risk reduction, 1486
change processes in self-help quitters, 1435
characteristics of quitters vs. continuing smokers, 0021
chronic obstructive pulmonary disease, effect on natural history, 0622
chronic obstructive pulmonary disease prevention trial, counseling efficacy, 1123
chronic pulmonary disease patients, treatment efficacy, 0137
college students, factors in successful self-quitters, 1272
communities in northern California, analysis of cessation contest, 0664
coping strategies in a social learning-based program, 6-month followup, 1377
coronary bypass surgery patients, efficacy of in-hospital intervention program, 1074
coronary disease patients, age, education, occupation as factors in success, 0299
coronary disease patients, effect on myocardial infarct and mortality, 1116
coronary disease patients, methods, 0581
coronary disease risk reduction, 0414
county health department cessation clinics in Tennessee, 1445
demographic characteristics of successful quitters, 1070
depression scores in ex-smokers, current smokers, smokers who want to quit, 0686
disease diagnosis as factor in long-term success, 0191
elderly persons, males vs. females, 0796
employee program, Allegheny County (Pennsylvania) Health Department, 1382
employees in American Lung Association worksite programs, 12-month followup, 1150
employees who watched antismoking videotapes at workplace, 0504
exercise level at 12 months, abstinence relationship, 1452
factory workers in China, efficacy of workplace program, 0148
Ford Motor Company employees, efficacy of multicomponent program, 1101
group cohesiveness as factor in cessation and reduction of smoking, 1547
head and neck cancer patients, reduced risk for second primary cancer, 0715
health and self-efficacy beliefs as success factors, 1457
health locus of control relationship, following bypass surgery, 1332
health professionals in Oregon, survey of antismoking efforts, 1366
Healthstyles program to promote health-enhancing behavior, 0074
heart disease prevention program, efficacy of nurse's intervention, 0528
heart study participants, self-quit methods and reasons, 1369
high school students in Italy, efficacy of health education program, 0336
hospital-based programs for staff and patients in Victoria, Australia, 0011
hospitalized patients with respiratory diseases, effect of antismoking advice, 0130
individual differences and attempts to quit following health education efforts, 1334
infertile men, estradiol production pre- and postcessation, 1098
inoperable cancer patients, individualized treatment program, 0785
insurance company employees, health promotion program utilizing spirometry, 1448
iron miners, lung function effects, 0221
ischemic heart disease, second event effect on behavior, with age and education, 1088
Kaiser-Permanente risk reduction program, self-help vs. group sessions, 0642
Kaunas-Rotterdam Intervention Study, for cardiovascular disease risk reduction, 0397
kibbutz members in Israel, health education by physician as factor, 0313
living with smokers vs. nonsmokers, effect, 1110
long-term smokers, brand-fading with/without behavioral training, efficacy, 1139
media campaign viewers in Western Australia, 0015
methodology for evaluating tobacco withdrawal programs, 0219
middle-aged men at risk for coronary disease, structured program success, 1100
middle-aged men, 1-year abstinence, efficacy of plastic cigarette vs. group therapy, 0154
Minnesota quit smoking contest, predictive factors for maintenance vs. recidivism, 1122
mortality reduction in smokers who quit or reduce use, 0287
Multiple Risk Factor Intervention Trial, success rates, 1419
myocardial infarct patients, long-term followup of effects on morbidity, mortality, 0300
myocardial infarct patients, psychosocial and demographic factors in success, 1086
myocardial infarct patients, program efficacy, 0399
nicotine-dependent smokers, efficacy of 2 mg vs. 4 mg nicotine gum, 1355
Normative Aging Study in middle-aged men, longitudinal effects, 1046
nurses' attitudes, motivation, and factors in recidivism, 0773
nurses in Minnesota, reasons for quitting and factors in recidivism, 1124
nurses in North Carolina, reasons for quitting vs. continuing smokers, 1326
oral cancer patients, risk reduction, 0702
oral melanin pigmentation, effect, 0476
participants in American Lung Association's clinic, quit rates 1983, 1218
participants in self-help program, efficacy of five approaches, 1267
patients and staff at hospital, program efficacy, 0967
patients of general practitioners, efficacy of nicotine gum vs. placebo gum, 0571
patients participating in an 8-week therapeutic program, 1300
patients receiving advice from nurse, with/without carbon monoxide test, 0548

patients with smoking-related diseases, 0593
perceived benefits and disadvantages, ex-smokers vs. smokers in Australia 1983, 0004
perceived personal vulnerability as factor, 1109
peripheral vascular disease patients, intervention program effectiveness, 1294
personality differences in smokers vs. ex-smokers vs. never smokers, long-term followup, 0670
persuasive communication to bolster intentions and confidence, 0524
physicians, personality correlates vs. continuing smokers, 1308
pilgrims to Indian temple, religious beliefs as factor, 0283
pregnant women, programs, 0634
psychological characteristics, abstainers vs. nonsmokers vs. smokers vs. recidivists, 1349
psychomotor task response inhibition during withdrawal, 1136
psychosocial stress and social support, long-term effects, 1378
pulmonary disease patients, predictive model, 0133
quit rates for current programs vs. earlier techniques, 0639
quitters vs. recidivists using self-help strategies, motivation as factor, 1065
recovering alcoholics, characteristics of quitters vs. recidivists, 1527
relapse episodes, cluster analysis and prediction of relapse situations, 1376
relapse factors in long-term maintenance, 1089
relapse prevention hotline for self-quitters, efficacy, 1289
relapse vs. abstinence, factors, 1094
self-efficacy as factor, 0046
self-quitters, 0576
sensation seekers vs. avoiders, essential program elements, 0788
sex-related differences, underlying factors and effect of clean indoor air laws, 1166
social background, type of smoker, family environment as factors in relapse, 1031
social network members, impact on cessation outcome, 1162
stressful life events, relationship, 0807
students in Moscow, effectiveness of intervention strategies, 0503
success as self-control measure, personal trait-like consistency, 1420
surgery patients, effect on postoperative morbidity, 0513
televised program viewers, 0507
three-stage theory to predict self-initiated cessation, 1335
university employees, comparison of three intervention strategies, 0607
university students, effect of counseling by health center physicians, 1283
veterans at medical center, self-efficacy as factor in program effectiveness, 1106
veterans at outpatient clinic, American Lung Association program, efficacy, 0747
volunteers in group counseling program, efficacy of aerobic exercise, 0135
withdrawal symptoms, gradual or abrupt cessation, effect on outcome, 1118
women in Sweden, effect on body weight, 0464
workers in Zambia, high cost and health concerns as reasons for quitting, 1563
worksite program participants, 0148
young, middle-aged, elderly men, effect on sex hormone levels, 0054

CESSATION OF SMOKING, METHODS
(*See also* REDUCTION OF SMOKING; WITHDRAWAL CLINICS)
ACS FreshStart group program, efficacy, 1194
acupuncture, efficacy, 0940
addictive smoking identification and nicotine gum, 0683
advice, plus booklet, plus placebo gum, plus nicotine gum, evaluation, 0593
aerobic exercise with group counseling, 0135
American Lung Association program, 0747
aversive smoking, 0739
behavior modification, 0179
biofeedback techniques, 0102
brand-fading, long-term efficacy, 1139
carbon monoxide feedback in group program, efficacy at 1, 12, 18 months postclinic, 0786
clinic programs in England and Wales, role of support services, 0553
communitywide smoking cessation contest, efficacy, 0664
company-sponsored multicomponent program, efficacy, 1101
computerized and individualized self-help program, 1220
computerized direct mail cessation materials vs. face-to-face program, efficacy, 1237
counseling and nicotine gum, efficacy, 0037
Five-Day Plan, reasons given for dropping out, 0209
four-phase media campaign in Western Australia, viewers' attitudes and response, 0015
"Freedom from Smoking in 20 days" television program, efficacy, 0855
gradual withdrawal, efficacy, 0836
health education program for military enlisted personnel in Italy, 0334
hospital treatment, withdrawal symptoms' effect on outcome, 1118
hypnosis, 0118
Kaiser-Permanente Stop Smoking Program, efficacy at 1-year followup, 0644
"Keys to Health" Finnish television series, efficacy, 0198
media and community interventions, evaluation, 0024
microcomputer-assisted relaxation program, smoking cessation component, 1075
minimal contact program at veterans medical center, efficacy, 1106
multidisciplinary program for physicians to use with patients, 0605
nicotine chewing gum, dosage requirements of nicotine-dependent smokers, 1355
nicotine chewing gum, efficacy, 0027
nicotine chewing gum, periodontal disease risk relationship, 1348
nicotine gum vs. behavioral treatment, efficacy for addicted smokers, 0866
nicotine gum vs. placebo gum, efficacy with/without physician's followup letter, 0600
nicotine gum with/without self-help manual for pulmonary disease patients, efficacy, 0137
nicotine vs. placebo chewing gum, 0663
nurse's advice with/without carbon monoxide test, efficacy, 0548
partner support/participation, efficacy with skills training, 1379
partner-support training with/without nicotine gum use, comparison, 0707
physician counseling, 0038 1091

plastic cigarette vs. group therapy in middle-aged men, efficacy at 1-year followup, 0154
prepaid medical plan program, 5-year followup, methodological evaluation, 0643
psychological and physiological treatment program utilizing nicotine chewing gum, 1099
QUIT program, characteristics of ex-smokers vs. recidivists, 0021
religious belief that smoking will result in punishment by God, efficacy, 0283
restricted environmental stimulation technique, with taped messages, efficacy, 1508
restricted environmental stimulation therapy (REST), efficacy, 0109
review of methods available in Switzerland, 0491
self help methods, 0191 0788 1385
social skills training for relapse prevention, efficacy, 0794
structured 5-day program for coronary-prone middle-aged men, 1100
televised cessation and behavior modification program in Finland, efficacy, 0201
televised series in Great Britain, 0507
therapist-conducted vs. self-administered, efficacy in hospital patients and employees, 1426
United States and Canada, review and evaluation 1978-1983, 0639
videocassette program for recovering myocardial infarct patients, efficacy, 0654
videotapes at workplaces, efficacy, 0504
withdrawal clinic for hospital staff, response, 0207
worksite programs, 0691

CHEWING TOBACCO
(*See also* TOBACCO CHEWING)
hamster embryo cells, cocarcinogenic effects with known carcinogens, 0412
olfactory aversion/covert sensitization procedure for cessation, 0749
sugar content, dental and periodontal disease relationship, 1405
tobacco-specific and volatile nitrosamines in Swedish samples 1981-1983, 0466

CHILDREN
aged 10 to 12 in Australia, factors associated with smoking, 0040
antismoking education in elementary schools, 1015
asthma and airway function in second and fifth graders, smoking and air pollution effects, 0723
asthmatic symptoms at age 7, smoking habits at age 21, 0022
asthmatics, smoking effect on pharmacological management, 0869
atherosclerosis risk factors, prevention program in Israel, smoking control as component, 0309
attitudes and viewpoints on smoking among elementary students in Japan, 0353
attitudes toward cigarette advertising, effect of viewing "Death in the West", 0709
attitudes toward smoking, tobacco production involvement as factor, 0957
behavior, attitudes, and beliefs about smoking, development in grades K-6, 0779
brain tumors, passive smoking as factor, 0733
clinical effects of drugs in hospitalized children, 1052
development at age 10, longitudinal study in Great Britain, parental smoking relationship, 1192
developmental effects of maternal alcohol use and smoking, 1023
developmental effects of maternal smoking, alcohol use, and lead exposure in pregnancy, 1344
difficult temperament as predictor of future marijuana, alcohol, and tobacco use, 1394
drug abuse, family effectiveness training for prevention, 0797
future drug use, etiologic determinants, 1248
health education about smoking, effect on initiation rates, 0235
health education by family physicians for 3- to 5-year-olds for prevention of smoking, 1476
health education for cardiovascular disease risk reduction, 1411
health education for prechoolers, effect on behavior, attitudes, beliefs, and values, 1482
health education for prevention of smoking, efficacy for students aged 10 to 12, 0589
health habits and behavior associated with coronary heart disease, longitudinal study, 0959
high school students as leaders of antismoking program for fourth graders, 1217
hyperactive, drug treatment effect on adolescent drug use and abuse, 0673
intellectual and behavioral development at age 7, effect of maternal smoking during pregnancy, 1391
intrauterine growth retardation, developmental effects, 0877
Know Your Body program for grades 4-6, replication and evaluation, 0780
leukemia and soft-tissue sarcoma, passive smoking as factor, 0317
lung function effects of early asthma and bronchitis, smoking factor, 0044
lung function, factors, 0049
maternal smoking in pregnancy, effect on development, 0071
My Body health education program in England, efficacy in prevention of smoking, 0568
passive smoke exposure measurement by expired carbon monoxide, 0569
passive smoking effects in asthmatic children, 0076
patterns and background factors in initiation of smoking, 0531
predictors of change in smoking status over time, peer influence, 1542
prevention of smoking programs, 0019
Primary Grades Health Curriculum Project, 1219
primary school students, effect of transfer to secondary school on smoking habits, 0596
respiratory effects of parental smoking and use of gas for cooking, 0870
respiratory system, long-term effects of passive smoke and air pollution exposure, 0435
respiratory tract diseases in infancy, parental smoking effect, 1287
rhabdomyosarcoma, parental smoking and other environmental factors in etiology, 1306
rural community in Nepal, smoking habits, 0393
sex differences in smoking habits in Perth, Australia, 0012
Smoke-Free Spaces for Kids, Canadian program to promote nonsmoking as the norm, 0069
smoking and health activity book for fourth and fifth grades, 0122

survey of smoking habits for program planning, Manitoba, Canada, 0081
third-year students in Dundee, Scotland, smoking habits, 0583

CHROMIUM
(*See also* METALS, METAL ISOTOPES)
metallic elements, carcinogenicity screening systems, 1258
soil and leaf levels on Ontario farms, 0062

CHROMOSOMES
aberration frequencies in hamster cells, effects of cigarette smoke, 0064
cytochrome P-450, effect of polycyclic aromatic hydrocarbons from cigarette smoke, 0443
cytogenetics, products of spontaneous abortion, maternal smoking factor, 1257
sister chromatid exchanges in lymphocytes of oral tobacco users, 1489
sister chromatid exchanges in occupationally exposed workers, 0177
sister chromatid exchanges, induction by low-, medium, and high-tar cigarettes, 0195
tobacco smoke components, mechanisms of action, 0488

Chronic bronchitis *See* BRONCHITIS

CHRONIC BRONCHOPULMONARY DISEASE
(*See also* BRONCHIAL DISEASES; EMPHYSEMA; LUNG DISEASES)
air pollution effects in smokers vs. nonsmokers, 0682
airway hysteresis in patients with smoking-related disease, 0679
biochemical indicators of alveolar destruction, 1296
C5 role in initiating influx of inflammatory cells, 0753
carboxyhemoglobin levels in transfused blood, risk relationship, 1152
ceruloplasmin and ferrous iron transferrin, roles, 1297
cessation of smoking in patients, treatment efficacy, 1436
chronic bronchitis in milk drinkers vs. nondrinkers, smoking as factor, 1007
chronic bronchitis vs. airways obstruction, differences in risk factors, 1005
detection and intervention program including smoking cessation, long-term followup, 1127
detection by spirometry following neon vs. air inhalation, 0633
elastase and α_1-antitrypsin imbalance in pathogenesis, smoking role, 0919
environmental factors, 0618
Hispanics vs. whites, smoking habit relationship, 1190
histamine and leukotriene levels in bronchial tree, relationship, 0181
hospitalized patients, smoking, occupation, and residence relationship, 0519
lifetime tobacco consumption correlation with incidence, 1037
male smokers, factors influencing progression, 0514
nicotine gum with/without self-help manual for smoking cessation in patients, efficacy, 0137
passive and active smoking as risk factors in Greek women, 0255
prevention trial, cessation of smoking advice effect on lung function decline, 1123
respiratory epithelium permeability in smokers vs. nonsmokers, 0651
urinary desmosine elevation in patients, 1147

wives of smokers, passive smoking risk relationship, 0280

CIGAR SMOKING
(*See also* Cigars)
bladder cancer risk relationship, 1009
lung cancer risk relationship vs. cigarette vs. pipe smoking, 0228
males in Switzerland, changes between age 19 and age 31, 0494
myocardial infarct and angina patients, effect on long-term morbidity, mortality, 0301
pancreatic, bile-duct, and gallbladder cancer risk relationship, 0246
periodontal health, effects vs. cigarette smoking, 1097

Cigarette butts *See* CIGARETTES; SMOKING CHARACTERISTICS

Cigarette holders *See* SMOKING ARTICLES

CIGARETTE SMOKE
(*See also* SMOKE INHALATION, ANIMAL; SMOKING)
absorbing material added to cigarettes to reduce level, 0864
activation of complement system and generation of complement-derived chemotactic peptides, 1281
active oxygens generation and resultant DNA strand breaks, effect, 0385
adenovirus types 5 and 7 and epithelioid cells, in vitro effects, 1169
airway receptors, response vs. nicotine aerosols, 0893
alpha radioactivity of smoke filtrates, 0865
alveolar macrophage transglutaminase inhibition, 1280
aromatic amines formation, influence of tobacco nitrate, 1202
aromatic hydrocarbons, induction of aryl hydrocarbon hydroxylase in rats, 0441
atherogenic effect of constituents in hamsters, 1203
carbon monoxide content, apparatus used by Federal Trade Commission for determination, 0777
chemical analysis of Indian lanka tobacco, 0268
chromosome aberration frequencies in hamster cells, effect with arsenic and chromate, 0064
cultured mesothelial and endothelial cells, cytotoxic effects, 0536
estrogen production of placental aromatase in rats, inhibitory effect, 1240
filter additives to remove harmful compounds, 0359
harman and norharman determination, tobacco alkaloid content relationship, 0822
immunogenicity and allergenicity of components, 0966
improvement and monitoring of smoke generating, manipulating, and exposure systems, 0894
instrumentation and methods for characterization, 1447
mainstream and sidestream condensates, effect on enzyme activity in rat lung and liver, 0343
mask and smoke dosage apparatus for inhalation studies in rabbits and small rodents, 0368
metabolic effects in pulmonary alveolar macrophages, 0338
mutagenicity in vascular cells, 1522
nonsmoking wives of smokers, lung cancer risk, 0254
oropharyngeal bacteria, effects of in vitro exposure, 1168
oxidative components, enzyme activity relationship in emphysema etiology, 0825

SUBJECT INDEX

Parkinson's disease, possible beneficial effect, 1251
pesticide residues, 1317
platelets, aggregation and release function, inhibition by carbon monoxide, 0623
radicals in gas phase smoke and tar, toxicity, 0961
size distribution of particulates, 0624
trace elements in Turkish cigarette tobacco vs. pipe tobacco vs. ash, 0499
white blood cell metabolism, effects, 0183

Cigarette smoke, gas phase *See* **GAS PHASE, CIGARETTE SMOKE**

Cigarette smoking *See* **SMOKING**

Cigarette tars *See* **TARS, CIGARETTE**

CIGARETTES
(*See also* TOBACCO)
advertising format and content effect on adolescents' brand preferences, 0695
advertising in New Zealand, public attitudes, 0403
alterations in structure to reduce smoke component yields, 0928
clove kreteks, implications of use by adolescents, 0106
consumption rates with administration of clonidine aminophylline or propranolol, 1506
design modification to reduce smoke levels, 0864
domestic and imported in Australia, tar, nicotine, and carbon monoxide levels, 0007
Egyptian, reduction in tar and nicotine content, 0173
filter vs. nonfilter, light vs. dark tobacco, lung cancer risk, 0228
high- vs. low-yield, effect with smoking characteristics on levels of smoke constituents, 0905
nitric oxide::tar ratios, current vs. 1970 cigarettes, 1447
plain vs. filter-tipped vs low-tar, cancer risk relationship, 0246
sales to minors in England, survey, 0516
tar and nicotine content of brands from developing countries, WHO-sponsored analysis, 0496
tar and nicotine content, myocardial infarct survival relationship, 0547
tar and nicotine content, short-term thermal treatment for tobacco expansion, effect, 0442
tar, carbon monoxide, and nicotine in British cigarettes, reduced levels, 0527
tar, nicotine, carbon monoxide levels in Italian cigarettes, 0331
taste, discrimination of own brand by smokers, 0795
tobacco industry liability in related fires, 0843
Turkish, trace elements in cigarette vs. pipe tobacco, 0499
urinary tract neoplasms, effect of type on etiology, 0344

CIGARETTES, HIGH-NICOTINE
cardiovascular effects vs. low-nicotine cigarettes vs. nicotine gum, 0681
prostacyclin and thromboxane balance in cardiovascular system, effect, 0668
smoke inhalation effects in dogs, 1180

CIGARETTES, HIGH-TAR
high- vs. low-tar, inhalation pattern changes, 0792
lung cancer risk relationship, 0050
smoke inhalation effects in dogs, 1180

CIGARETTES, LOW-NICOTINE
cardiovascular effects vs. high nicotine cigarettes vs. nicotine gum, 0681
prostacyclin and thromboxane balance in cardiovascular system, effect, 0668
smoke inhalation effects in dogs, 1180

CIGARETTES, LOW-TAR
adolescent smoking initiation in Great Britain, effect with advertising, 0505
biochemical effects in former high-tar cigarette smokers, 0533
filter with acceptable pressure drop to retain taste, 0383
high- vs. low-tar cigarettes, inhalation pattern changes, 0792
lung cancer risk reduction in smokers, 1216
lung cancer risk relationship vs. high-tar cigarettes, 0050
sister chromatid exchanges, induction by condensate vs. medium- and high-tar cigarettes, 0195
smoke inhalation effects in dogs, 1180

CIGARETTES, LOW-YIELD
bronchial histologic changes, relationship, 1177
compensatory smoking in smokers who switch, 1215
design and manufacture for research purposes, 0932
health effects compared with high-yield brands, 0641
lung cancer mortality, lower tar intake effect, 0039
mutagenicity and carcinogenicity of flavor additives, 1198
myocardial infarct and cancer epidemiology relationship, 1299
nicotine, cotinine, carbon monoxide levels in brand switchers, 1017
Turkish tobacco with very high nicotine/moderate tar, applicability, 1447
voluntary brand switchers, smoking pattern changes, 1016

CILIARY ACTIVITY
(*See also* PULMONARY CLEARANCE)
chronic bronchitis patients, sputum production and clearance in smokers vs. ex-smokers, 0550

Cirrhosis, liver *See* **LIVER CIRRHOSIS**

COCARCINOGENS
(*See also* CARCINOGENS)
catechol, effect on DNA-binding of (^{3}H)benzo(*a*)pyrene to mouse skin, 1212
cigarette smoke extracts, with environmental and occupational carcinogens, 0412
metabolism and effects on carcinogenic polycyclic aromatic hydrocarbons, 0862
radon daughter and smoking in lung cancer etiology in uranium miners, 0656

COFFEE CONSUMPTION
(*See also* CAFFEINE)
alcohol use, smoking, and stress as predictive factors, 0134

bladder cancer relationship, with smoking, 0091
chronic bronchitis vs. airways obstruction, risk relationship, 1005
drug abuse research study, relationship with smoking and alcohol use, 0991
morbidity risk in smokers vs. nonsmokers, 0998
neonatal effects of maternal use, with smoking, 0117
pregnant women, fetal effects, 1262
puffing behavior of inhalers vs. noninhalers, relationship, 0485
relationship to smoking under laboratory conditions, 0996
ulcerative colitis risk relationship, 1537
urinary cancer risk factor, with smoking, 0344
urothelial cancer risk relationship in Japanese, with smoking, 0829

COGNITION
(*See also* LEARNING; MEMORY; PERCEPTION)
cessation of smoking program element for relapse prevention, 1435
child at age 10, parental smoking relationship, 1192
complex problem-solving tasks, smoking effect on performance, 1066
health benefits of smoking cessation, belief as factor in maintaining abstinence, 0525
health effects of smoking, effect on smoking behavior, 0562
information processing, nicotine and smoking effects, 0574
letter cancellation task, performance by high vs. low arousal situation smokers, 0579
religious belief that God will punish smokers as factor in cessation, 0283
self-report questionnaire, discrimination of smoking status by cognitive orientation, 1513
seventh graders, smoking prevention curriculum, factor in efficacy, 1234
tone discrimination task, smoking vs. nonsmoking condition effect on performance, 0484

College students *See* STUDENTS

COLON
(*See also* INTESTINES)
nicotine chewing gum for treatment of ulcerative colitis, efficacy, 1239
ulcerative colitis risk with tobacco, coffee, and alcohol consumption, 1537

COLONIC NEOPLASMS
diet, alcohol consumption, and tobacco use as risk factors for large bowel cancer, 0033
Nebraska Laboratory Cancer Research Center, research objectives, 1154

Common cold *See* **RESPIRATORY TRACT INFECTIONS**

Congenital defects *See* **BIRTH DEFECTS**

CONTRACEPTIVES, ORAL
cancer and cardiovascular disease in women, risk relationship, 1078
cervical dysplasia risk relationship, with smoking, 0124
fibrinolysis in rats, effect of injections, with smoke exposure, 0451
fibrinolytic activity of vein walls in long-term users, smoking effect, 0450
liver cancer risk relationship, with smoking, alcohol consumption, and other factors, 0732
mortality in users, smoking relationship, 0549
myocardial infarct risk factor, synergistic effect with smoking and hypertension, 1053
myocardial infarct risk relationship in women under age 50, smoking as factor, 1039
pregnancy risk factor, with abortion and smoking, 0772
prostacyclin activity in smooth muscle cells, effect with smoking, 0321
selenium concentrations in blood, effect with alcohol consumption, age, and smoking, 0577

COPPER
(*See also* METALS, METAL ISOTOPES)
abdominal aortic aneurysm, role with smoking in etiology, 0631
soil and leaf levels on Ontario farms, 0062
tobacco grown on sludge-amended soil, levels, 1030

Coronary arteriosclerosis *See* **CORONARY DISEASE**

CORONARY DISEASE
(*See also* ANGINA PECTORIS; HEART DISEASES)
adults in Dundee, Scotland, smoking habit relationship, 0583
adults in Finland, cessation of smoking and mortality relationship, 0201
air crewmen, risk factor determination, 1465
aluminum industry workers in Quebec, occupational exposure and smoking as risk factors, 0087
artery spasm in patients, smoking relationship, 0887
behavioral and physiological risk factors, 5-year followup study, 1277
blood circulation in patients, smoking effect, 0888
bypass surgery patients, efficacy of in-hospital smoking cessation program, 1074
carbon monoxide exposure of patients, acute effects in nonsmokers, 0649
cessation of smoking in acute episode patients, age, education, occupation as factors, 0299
cessation of smoking in patients, methods, 0191
cessation of smoking in patients, long-term effects on morbidity, mortality, 0300
cessation of smoking influence on myocardial infarct and mortality, 1116
cholestyramine and diet treatment of arterial disease patients, 5-year program, 1416
etiology, acute manifestations, short-term prognosis in smokers, 0298
health decision model as basis for cessation program for angina patients, 1496
health education for hospitalized patients, efficacy of individualized approach, 0581
health habits and behavior in children, longitudinal study of relationship, 0959
high-risk men who smoke, cessation program effectiveness, 1100
hospital patients in Barbados, smoking habit relationship, 0053
intervention program, smoking and diet as risk factors, 0414

intervention trial in Sweden, 10-year followup data on risk factor reduction, 0473
ischemic heart disease, second event effect on smoking behavior, with age and education, 1088
Japanese males born and living in Hawaii, smoking and other risk factors, 0828
Know Your Body program for grades 4-6, for prevention, 0780
mortality and morbidity in patients following angioplasty, smoking effect, 1423
mortality in breast cancer patients with/without radiotherapy, factors, 1067
mortality in Israeli cohort, 15-year followup, 0308
mortality in middle-aged men, risk factors, 0676
mortality in twin pairs in Finnish cohort study, smoking as factor, 0203
mortality in veterans, ratios for smokers vs. nonsmokers, 1011
Multiple Risk Factor Intervention Trial, coordinating center, 1129
Normative Aging Study in middle-aged men, factors, 1046
North Karelia intervention program, effect on smoking habits, 0197
physical activity and fitness, risk relationship, 0058
platelet thrombosis and clotting in etiology, smoking effect, 1554
population-based study of long-term predictors, smoking as risk factor, 0698
prevention trial, validity of self-reported smoking behavior, 0057
psychosocial factors, effect on outcome, 1305
risk factor incidence relationship to educational level, 0297
risk factors in smokers vs. nonsmokers, 0252
selenium and vitamin E in relation to risk factors, smoking role, 0578
smoking as risk factor, 0534
social and physical variables affecting future risk, 0420
students in Moscow, risk factor assessment for early detection, 0503
women, incidence in smokers vs. nonsmokers, Framingham study participants, 0987

Coronary flow *See* **BLOOD CIRCULATION**

Coronary thrombosis *See* **CORONARY DISEASE**

Coronary vessels *See* **BLOOD VESSELS**

Corpulmonale *See* **PULMONARY HEART DISEASE**

COST BENEFITS ANALYSIS
(*See also* ECONOMICS; TOBACCO INDUSTRY)
absenteeism in Czechoslovakian plant, smokers vs. nonsmokers, 0153
blood tests vs. x ray vs. sputum tests for early detection of lung cancer, 0116
cessation of smoking, sex, age, and amount smoked as factors, 1079
chronic illness and absenteeism, smoking relationship, 0543
communitywide smoking cessation contest in northern California, 0664
economic benefits and losses from cigarette smoking in various countries, 0128
interagency smoking cessation program for pregnant women, 0634
intervention program for pregnant smokers to reduce low birth weight infant care costs, 1141
Lifecycle model of preventive health services, 1242
no smoking policies in workplaces, 1279
prevention of smoking curriculum, maximum vs. minimum teacher support, 1235
self-help approaches to smoking cessation, evaluation of three programs, 1322

COTININE
(*See also* ALKALOIDS, TOBACCO; NICOTINE DERIVATIVES)
blood and urine levels in smokers who switch from high- to low-tar cigarettes, 0533
distribution and kinetics in pregnant sheep and fetus, 0672
lanka tobacco of India, level in leaf and smoke, 0268
NAD(P) glycohydrolase role in exchange reaction with nicotinamide, 1050
passive smokers vs. smokers vs. nonsmokers, 0194
plasma levels, cigarette yield, smoking history, and smoking behavior as determinants, 0905
plasma levels in brand switchers, 1017
radioimmunoassay for determination in blood, urine, saliva, and other samples, 1049
schedule-controlled responding in dogs and squirrel monkeys, effect, 1014
serum levels in pregnant women, measurement to encourage smoking reduction, efficacy, 0969
tumor development in rats, effect with nicotine-N'-oxides, 1210
umbilical cord and maternal blood levels, smokers vs. nonsmokers, 0379
urinary levels in nonsmokers, passive smoking relationship, 0245
urinary levels in smokers and nonsmokers, exposure measurement, 0380
urine and plasma concentration as smoking status determinant, 0215
urine and plasma levels in smokers vs. nonsmokers, 0375
urine levels, effect of renal function impairment, 1433
urine levels in infants, passive smoking exposure indicator, 1327

COUGH
(*See also* RESPIRATORY SYMPTOMS)
females in Hong Kong, lung cancer risk factor, 0258
prevalence in smokers vs. ex-smokers vs. nonsmokers, 0560
smoking-related respiratory symptoms in men vs. women, 0234
withdrawal symptom following smoking cessation, 0026

COUNSELING
(*See also* CESSATION OF SMOKING, METHODS)
adolescents, prevention/intervention program for smoking and drug abuse, 1421
cancer intervention and prevention program for high-risk community, 1387
coronary disease patients, individualized health education, efficacy, 0581
doctors and dentists, cessation of smoking method, efficacy, 0861
family clinic physicians, 2-hour training program on cessation by patients, efficacy, 1268
general and subspecialty internists, advice to patients about smoking and exercise, comparison, 0697
hospital personnel antismoking advice, efficacy with respiratory disease patients, 0130

individualized in comprehensive health care setting, efficacy for smoking cessation, 1502
lung disease patients, effectiveness in cessation of smoking, 0133
nurses for smoking cessation, with/without carbon monoxide test, efficacy, 0570
physicians for smoking cessation, 0037 0614
physicians, patient's age, sex, and health status, effect on intervention practices, 1084
pregnant women during obstetric care, efficacy for smoking cessation, 1504
residents in family medicine, educational training program on smoking risks and cessation, 0761

Crotonaldehyde *See* ALDEHYDES

CYANIDES
rhodanese activity in tobacco amblyopia, 0556

CYTOCHROMES
monoclonal antibody-directed phenotyping of P-450 in animal and human tissues, 0990
P_1-450 activity in smokers vs. nonsmokers, breath test with caffeine demethase, 0848

Death rates *See* MORTALITY

Deformities *See* **BIRTH DEFECTS**

DEMOGRAPHIC FACTORS
(*See also* AGE FACTORS; ETHNIC GROUPS; SEX RATIO)
cancer epidemiology in California Mormons, relationship, 0684
cancer incidence, with smoking and alcohol consumption, 0492
cancer mortality in France, relationship, 0231
cancer mortality relationship in Poland, 0433
cancer patients, epidemiology data system, 1269
cancer patients, with smoking and personality, 0566
cerebral tumor etiology, 0093
cessation of smoking methods most effective for different smoker subpopulations, 1170
coronary artery disease patients, baseline characteristics in 5-year treatment program, 1416
hospital patients on Connecticut Tumor Registry, 0770
Mormon nonsmoking life style, adherence relationship to cancer incidence, 1019
mortality risk factors in urban and rural areas of Shanghai, 0145
myocardial infarct patients, cessation of smoking relationship, 1086
National Survey of Family Growth, 0981
nurse practitioners, effect on antismoking activities with patients, 0771
nurses with master's degree, smoking habit relationship, 1422
population subcategories in Canada, variations in smoking over time, effect, 0061
pregnant women, effect on outcome, 0077
smokers vs. ex-smokers vs. recidivists vs. nonsmokers, 1070
tobacco use and myocardial infarct and cancer risk, relationship, 1299
urban vs. rural residence, effect on chronic bronchitis incidence, 0427
Washington State risk control survey, 1540

DENTAL DISEASES
(*See also* PERIODONTAL DISEASES)
adolescents in Sweden, smoking and snuff use relationship, 0456
adolescents, smokeless tobacco use association, 0756
chewing tobacco use relationship, 1405
cigarette, pipe, and cigar smokers, differential effects, 1097
smokeless tobacco use, risk relationship, 0819

Dental hygiene *See* **ORAL HYGIENE**

Deoxyribonucleic acid *See* **DNA**

Deoxyhemoglobins *See* **HEMOGLOBINS**

DIABETES
(*See also* BLOOD SUGAR)
adolescent, cardiovascular disease risk evaluation, 1417
blood circulation deterioration in patients, smoking as factor, 0139
high-cholesterol diet and experimentally induced diabetes, atherogenic effect in rats, 0745
Japanese-American men, smoking and other factors in etiology, 1528
microcirculation in smokers vs. nonsmokers, 0140
middle-aged men in Sweden, heart disease and cancer mortality risk, with smoking, 0474
myocardial infarct patients, effect on platelet aggregation, 0608
nicotine-induced hyperglycemia in diabetic vs. healthy smokers, 0141
plasma lipoproteins and cholesterol-binding, with smoking in disease severity, 0954
pregnant women, red cell oxygen transport and release, smokers vs. nonsmokers, 0156
retinopathy in patients, smoking as factor, 0239

DIBENZANTHRACENE
(*See also* AROMATIC HYDROCARBONS)
aromatic hydrocarbon dihydrodiol derivatives, carcinogencity, 0190

DIET
animal vs. vegetable fats as cancer risk factors, with tobacco use, alcohol consumption, 0246
antioxidant intake effect on carcinogenicity of tobacco smoke in hamsters, 0367
Arab and Jewish adolescents in Israel, with smoking and other health-related behaviors, 0306
cancer and cardiovascular disease is women, risk relationship, 1078
cancer patients, epidemiology data system, 1269
cancer risk relationship, 0684
carcinogen activation effect, 1027
cardiovascular disease risk factor in nurses, with smoking, 1054
carotene-containing foods, effect on lung cancer risk, 1276
characteristics of smokers vs. nonsmokers vs. ex-smokers, 0350
cholesterol-enriched, effect with smoke inhalation in rabbit ears, 0372
coronary artery disease patients, with cholestyramine in 5-year treatment program, 1416
coronary bypass patients, effect on arteriosclerosis in nonsmokers, 0719
coronary heart disease risk factor with smoking, intervention program, 0414

DNA single-strand breaks, factor with age and smoking, 0174
elderly women, hematological effects, with smoking, 0885
health education for cardiovascular risk reduction in children and parents, 1411
health promotion program for villages in Finland, 0205
Healthstyles program to promote health-enhancing behaviors, 0074
high-cholesterol diet and experimentally induced diabetes, atherogenic effect in rats, 0745
high-fat diet and smoke effects on lung tissue morphology in monkeys, 0868
Hispanic Health and Nutrition Survey, 0978
hypertension, factors in etiology among adolescents, 1444
ischemic heart disease relationship, with smoking, 0598
Japanese-American men, factor with smoking in diabetes mellitus, 1528
Japanese men born and living in Hawaii, coronary disease risk relationship, 0828
Kuopio Ischaemic Heart Disease Risk Factor Study, 0204
lactation and infant growth effects, with smoking, 1525
large bowel cancer risk relationship, with tobacco use and alcohol consumption, 0033
lipoprotein lipase activity as factor in overweight dieting smokers vs. nonsmokerss, 0762
lung cancer risk relationship, 0034
lung, stomach, and pancreatic cancers relationship, with smoking, 0960
multiple myeloma epidemiology, with smoking and other factors, 1310
National Health and Nutrition Study, 10-year followup, 0976
North Karelia Youth Project to prevent smoking and improve diet of 12- to 16-year-olds, 0200
oral cancer risk factor, with alcohol consumption and smoking, 0032
oral, laryngeal, esophageal cancers, risk factor with smoking, 1520
pancreatic cancer risk relationship, with alcohol consumption, smoking, and family history, 0036
pregnant women, birth weight effects, with smoking, surveillance system, 0815
pregnant women, effect on outcome, 0077
pregnant women, relationship between dietary intake and biochemical indices of nutrition, 0555
reliability of long-term recall in prevention programs, 0661
respiratory cancer, nutritional and smoking correlations to occupational risk, 0665
saturated fat intake in Scottish farmers, additive effect with smoking on platelet function, 0229
stress modification, with alcohol consumption and smoking, in household populations, 1265
submucous fibrosis and oral carcinoma in South African Indians, factor with betel nut chewing, 0446
urinary conjugate levels, drugs and smoking effect, 1510
vitamin E and beta-carotene for cancer prevention, U.S.-Finnish trial, 0986
worksite cessation program, factor in abstinence, 0691
zinc supplements for smokers to counteract cadmium intake effects, 1236

DNA
- (*See also* RNA)
- adducts analysis method for carcinogens, 1460
- age-related alterations in single-strand breaks, smoking and diet as factors, 0174
- benzo(*a*)pyrene binding, 0862
- benzo(*a*)pyrene diolepoxide-DNA adducts as lung cancer risk, 0982
- benzo(*a*)pyrene effects on levels in pancreatic tissue, 0827
- benzo(*a*)pyrene metabolism in oral mucosa cells, reaction with DNA, 0158
- carcinogens, immunological techniques to study interactions, 0984
- enzymes in removal of O^6-methylguanine from methylated DNA, 1155
- genetic improvement of leaf safety, 1033
- (^{3}H)benzo(*a*)pyrene metabolism and binding, effects of catechol, 1212
- ^{3}H-dibenzo(*c, g*)carbazole binding, 1359
- metallic elements effects on repair, carcinogenicity mechanisms, 1258
- nicotine and benzo(*a*)pyrene effects on cellular DNA, 1064
- nitrosamine carcinogenesis, biochemical mechanisms, 1353
- nitrosamines, adduct formation in metabolism and carcinogenesis, 1205
- nitrosamines in tobacco smoke administered to nursing rats, effects in sucklings, 0001
- phenotypic analysis of epithelial cell neoplastic progression, etiologic relationship, 1507
- placental binding and benzo(*a*)pyrene metabolism, smoking effect, 0216
- strand breakage as measurement of damaging agents in cigarette smoke, 0488
- strand breaks, relationship to cigarette smoke generation of active oxygens, 0385
- tobacco smoke condensate fractions, effect on single-strand breaks, 0178

Dobutamine *See* CATECHOLAMINES

Dopa *See* CATECHOLAMINES

Dopamine *See* CATECHOLAMINES

DRUG ABUSE
- (*See also* CANNABIS)
- adolescents, factors, 0995
- adolescents, prevention programs, 0726
- birth defects association, with maternal smoking, 1043
- children grades K-6, developmental factors, 0779
- children, Primary Health Curriculum Project, followup study, 1524
- cocaine, interaction with alcohol, tobacco, marijuana, and diazepam use, 0847
- coffee, alcohol, and cigarettes as related habits vs. heroin and cocaine, 0991
- family effectiveness training for prevention, 0797
- female college students, fathers' influence, 1222
- heredity and environment as factors, twin study, 0754

heroin addicts, buprenorphine treatment effect on cigarette smoking, 1056
high school students in Italy, smoking and alcohol consumption relationship, 0342
hyperactive adolescents, pattern and progression of use, 0673
inner-city junior high school students, perceived neighborhood setting as factor, 0798
intervention strategies for sixth, seventh, and eighth graders, evaluation, 0727
marijuana, typography and dose regulation in adolescent and adult users, 0706
morbidity and mortality relationship in Barbados, 0053
mortality 1980, with smoking, alcohol consumption, 0971
Napa Drug Abuse Prevention Project, evaluation of school-based programs, 0647
nicotine as a prototypic dependence-producing drug, 1012
pregnant women, effect on outcome, 1038
prevention/intervention services for children of substance-abusing families, 1493
tobacco as hallucinogenic and narcotic agent in pre-Columbian Aztec culture, 0400
tolerance and dependence, biochemical factors, psychosocial interventions, 0704

DRUG METABOLISM
buprenorphine treatment for heroin addicts, effect on cigarette consumption, 1056
clinical effects of drugs in hospitalized children, 1052
cocaine and nicotine self-administration in dogs, schedule effect on behavior, 1013
deposition and sensitivity in smokers vs. nonsmokers, 1080
hydroxyethylrutosides, effect on smoking-induced changes, 1146
methacholine, airway response to inhalation in nonsmokers vs. smokers, 0277
metoprolol and propranolol in persons with minimal airway disease, 0621
parameters for determining smoking status, 0215
pharmacologic management of asthmatic children, smoking effect, 0869
phencyclidine, interactive effects with 1-phenylcyclohexene in rats, 1340
phenytoin and propranolol, protein binding in serum, smoking effect, 0899
psychotropic drugs in rats and rhesus monkeys, interactive behavioral effects, 0357
ranitidine and cimetidine plasma levels and elimination half-life, smoking effect, 0580
subjective effects in animals, pharmacological and psychological mechanisms, 1406
theophylline, inhibition by cimetidine, smoking effect, 0834
tolbutamide in smokers vs. nonsmokers, 0282
tolerance levels, biochemical factors, 0704
tuberculosis patients given isoniazid, lung cancer risk with smoking, 0508

Duodenal ulcer *See* **PEPTIC ULCER**

DUST
lung clearance rate in smokers vs. nonsmokers, 1076
lung damage from inhaled toxins in cotton dust and cigarette smoke, 1309
mutagens in sputum from occupationally exposed workers, smokers vs. nonsmokers, 0422
occupational exposure and smoking in coal miners, lung disease risk relationship, 1545
tobacco factory, acute and chronic diseases in exposed workers, 0167

EARS
acute otitis media with effusion in infants, passive smoking relationship, 1324
cholesterol-enriched diet and smoke inhalation in rabbits, effects, 0372
sensory input regulation, nicotine effects, 0031

ECONOMICS
(*See also* COST BENEFITS ANALYSIS; TOBACCO INDUSTRY)
cost benefit analysis of cigarette smoking in various countries, 0128
cost of smoke-free areas in workplaces, information kit, 0063
Finland, simulation model for analyzing policy options for reducing smoking, 0199
no smoking policies in workplaces, benefits, 1279
quarterly publication, issues affecting the tobacco industry, 1270
tobacco industry, current outlook by U.S. Department of Agriculture, 0784
tobacco price, consumption, and product weight, relationship, 0080
Zambia, high cost of cigarettes as reason for quitting, 1563

ELECTROCARDIOGRAPHY
cigarette smoke effects on cardiac electrophysiology, 1036

ELECTROENCEPHALOGRAPHY
right vs. left cerebral hemisphere activity in abstinent smokers, 0744

EMBRYO
maternal occupational exposure to metallic mercury, reproductive effects, 0086
nicotine effects on development in the rat, 1111

EMPHYSEMA
(*See also* CHRONIC BRONCHOPULMONARY DISEASE; OBSTRUCTIVE AIRWAY DISEASES)
alveolar hypoxia relationship, 1138
apical localization, role of particle deposition during cigarette smoking, 0136
bacterial adherence in colonization of airways of patients, smokers vs. nonsmokers, 1249
biochemical indicators of alveolar destruction, 1296
carbamate inhibitors of elastase, therapeutic potential, 0902
changing incidence in long-term smoke-exposed dogs, 1178
elastase activity in etiology, 0919
elastase-induced in hamsters, smoke inhalation effects, 1226
elastolytic activity of leukocytes and alveolar macrophages in etiology, 1117

long-term exposure to cigarette smoke as factor, 1407
morphologic changes in respiratory system of smoking dogs, etiologic relationship, 1179
mortality in veterans, ratios for smokers vs. nonsmokers, 1011
nicotine and cigarette smoke particulates in etiology, toxicological investigation, 0900
proteoglycan chemistry and function in pathogenesis, smoking effect, 0962
proteolytic enzymes in etiology, relationship of oxidative components of smoke, 0825
puffing characteristics of smokers, relationship, 0489
pulmonary alveolar macrophages in hamsters, relationship, 1450
smoke-exposed dogs, relationship to tar and nicotine levels, 1180

ENDOCRINE FUNCTION
disturbances induced by nicotine and smoking in male and female rats, 0454
neuroendocrine cell innervation in neonates, maternal smoking effect in hamsters, 1555
nicotine and carbon monoxide effects in humans, 0746
smoking effect on thyroid hormones, 0458

Environmental pollution *See* **AIR POLLUTION**

ENZYME ACTIVITY
age, smoking, alcohol consumption in the elderly, effects, 0218
alpha-1-proteinase inhibitor:elastase balance in the lung, smoking effect, 1407
alpha$_1$-antitrypsin concentration and activity, smoking effect, 0224
alpha$_1$-protease inhibitor in bronchoalveolar lavage fluid, smoking effect, 0115
alveolar macrophage elastolytic activity in current smokers vs. ex-smokers, 0302
aryl hydrocarbon hydroxylase in mice, 0430
aryl hydrocarbon hydroxylase in rats, 0441
atherosclerotic lesions, effect with tobacco smoke, 1526
benzo(*a*)pyrene effects in pancreatic tissue, 0827
benzo(*a*)pyrene-induced pulmonary neoplasms, carcinogen-metabolizing activity, 0872
benzo(*a*)pyrene metabolism in the ovaries, effect on reproductive function, 0626
benzo(*a*)pyrene metabolism, factor in carcinogenesis, 0042
bioactivation and detoxification of potential toxic compounds, 1453
biochemical indicators of alveolar destruction, 1296
carcinogen activation in liver and lung, 1027
circulating pancreatic proteases and aortic aneurysm in aged heavy smokers, 0734
cytochrome P-450 system in benzo(*a*)pyrene carcinogenesis, 0354
deoxyguanosine-BaP and deoxyadenosine-BaP adducts, removal from DNA, 1155
DNA strand break inhibition in cancer cells following incubation with cigarette smoke, 0385
elastase activity in bronchoalveolar lavage fluid, smoking effect, 0111
elastase and myeloperoxidase, chronic cigarette smoking effect, 0908
elastase and trypsin inhibiting capacity in plasma, smoking effect, 0110
elastase in emphysema etiology, 0902
estrogen production by placental aromatase in rats, inhibition by tobacco components, 1240
glutathione peroxidase activity in blood, factors, 0577
heat-stable alkaline phosphatase, activation in smokers, nonsmokers, cancer patients, 0637
heat-stable alkaline phosphatase in nonsmokers, as tumor marker, 0636
hepatic enzyme activity in smoke-exposed rats, stress effect, 0889
human placenta, inhibition by monoclonal antibodies to methylcholanthrene-P-450, 0990
induction of hepatic caffeine demethase in smokers to measure P$_1$-450 activity, 0848
lung and liver induction in rats, effect of smoke condensates, 0343
lung GMP fluctuations, guanylate cyclase response to gas phase cigarette smoke, 1352
lung permeability in smoke-exposed hamsters, elastase injection effect, 1119
lung tumorigenesis in mice, role of beta-glucuronidase and inhibitors, 1354
lysosomal enzymes in smokers vs. nonsmokers, 0107
lysyl oxidase in aortic aneurysm etiology, smoking role, 0631
modulation of extracellular neutrophil elastase activity, 1140
myeloperoxidase and others in neutrophils of noise-exposed workers, smoking effect, 0438
N-nitrosodimethylamine-hydroxylase activity, potentiating effects of sex hormones in mice, 0781
neutrophil elastase in emphysema induction, 0825
nicotine and cotinine, role of NAD(P) glycohydrolase in exchange reactions, 1050
obstructive airways disease, smoking effect, 0913
oxidases and hydrolases in tobacco leaf constituents during air curing, 0891
P450 activation of nitrosamines, biochemical mechanisms of carcinogenesis, relationship, 1353
pancreatic carcinogen-metabolizing enzymes, 0871
placenta, smoking effect on metabolism, 0211
placental detoxification systems, response to maternal smoking, 0758
placental multiple mixed-function oxidases, maternal smoking as inductive stimulus, 1346
plasma neutrophil elastase release following acute smoking, 0113
polycyclic hydrocarbons, activation in liver, role in carcinogenesis, 1157
porcine pancreatic elastase and cigarette smoke effects in rat lung, 0900
prostacyclin synthetase in vascular bed, relationship with smoking in coronary disease etiology, 0500
proteases and antiproteases, role in coal workers pneumoconiosis, 1247
proteoglycan catabolism in bronchoalveolar lavages in baboons, smoking effect, 0962
pulmonary alveolar macrophage biochemistry, cigarette smoke effect, 0338
rhodanese in tobacco amblyopia and Leber's disease, 0556
serum inhibitory activity against trypsin and elastase, chronic smoking effect, 0906
squamous cell carcinoma of the oral cavity, role of gamma-glutamyltranspeptidase, 0841

steroidogenic enzymes, synthesis of progesterone and estrogens in pregnancy, 0392
testicular androgen hydroxylases, pubertal, smoking, and dioxin effects, 1186
tracheal ciliated cells from rabbits, mixed-function oxidase activity, 1316
transglutaminase in rabbit alveolar macrophages, inhibition by cigarette smoke, 1280
tryptophan hydroxylase in brain tissue, 0584
upper vs. lower lobes, elastase levels and alpha$_1$-antiprotease activity, 0114
urinary excretion of D-glucaric acid for measurement, effect of age, sex, smoking, 0340
weight loss in dieting smokers vs. nonsmokers, lipoprotein lipase activity relationship, 0762

ENZYMES
(*See also* ARYL HYDROCARBON HYDROXYLASE)
alkylguanine alkyltransferase, 1155
alpha$_1$-antitrypsin, 0224
alpha$_1$-protease, 0913
amylase, 1296
antiprotease, 1044
aromatase, 1240
aryl hydrocarbon hydroxylase, 0441
beta-glucosaminidase, 0107
beta-glucuronidase, 1354
caffeine demethase, 0848
carbon monoxidase, 1303
catalase, 0385
coumarin hydroxylase and 7-ethoxycoumarin deethylase, 1316
cytochrome P-450, 1453
cytochrome P-450 isozymes, 0872
cytochrome P-450 monooxygenases, 0758
elastase, 0110 1140
epoxide hydrolase, 0758
gamma-glutamyltranspeptidase, 0841
glutathione peroxidase, 0577
glutathione S-transferase isozymes, 0872
glutathione S-transferases, 0758
guanylate cyclase, 0740
heat-stable alkaline phosphatase, 0636
hydrolases, 0891
lipoprotein lipase, 0762
lipoxygenase, 0919
lysyl oxidase, 0631
myeloperoxidase, 0908
NAD(P) glycohydrolase, 1050
NADPH-cytochrome P-450 reductase, 0872
neutrophil elastase, 0825
neutrophil lysosomal elastase, 1259
ornithine decarboxylase, 0827
oxidase, 0891
pancreatic proteases, 0734
porcine pancreatic elastase, 0900
prostacyclin synthetase, 0500
proteases, 1247
rhodanese, 0556
steroidogenic, 0392
superoxide dismutase, 0385
topoisomerase, 1155
transglutaminase, 1280
trypsin, 0110
tryptophan hydroxylase, 0584

Epidermoid carcinoma *See* **CARCINOMA, EPIDERMOID**

Epinephrine *See* **CATECHOLAMINES**

Epithelial cells *See* **CELLS, EPITHELIAL**

ERYTHROCYTES
(*See also* BLOOD; HEMATOCRIT; HEMOGLOBINS)
deformability, acute tobacco intoxication effect, 0439
micronucleated and polychromatic, effect of chemicals in bone marrow, 0386

ESOPHAGEAL NEOPLASMS
(*See also* GASTROINTESTINAL NEOPLASMS)
alcohol consumption and N'-nitrosonornicotine treatment in rats, interactive effect, 1204
alcohol consumption, diet, occupation, dental hygiene, smoking as risk factors, 1520
diet, alcohol consumption, tobacco use as factors, 0032
endoscopic screening of high-risk patients, 0356
high-risk populations, risk factor determination, 0989
mortality, alcohol consumption and smoking, risk relationship, 0564
Nebraska Laboratory Cancer Research Center, objectives, 1154
nitrosamine carcinogenicity promoted by catechol in rats, 1160
rural African population, tobacco use as risk factor, 0445
snuff and chewing tobacco use, relationship, 0988
tobacco and other environmental factors, 0858
women in India, snuff use relationship, 0269

ESOPHAGUS
(*See also* GASTROINTESTINAL SYSTEM)
endoscopic survey of dysplasia in high-risk patients, 0856

ETHNIC GROUPS
(*See also* DEMOGRAPHIC FACTORS)
Amish, lung cancer mortality vs. non-Amish population, nonsmoking as factor, 1398
Arab and Jewish adolescents in Israel, smoking and other behaviors, 0306
black vs. white women, prenatal care and smoking as factors in birth weight, 1141
blacks in inner city, smoking and perceived health status, relationship in the elderly, 1175
blacks vs. whites, alcohol consumption as stress modifier, with smoking, 1265
blacks vs. whites, glaucoma risk factor study, 0999
California Mormons, lifestyle factors in cancer epidemiology, 0684
cancer incidence in Hawaii, risk factor identification survey, 0830
Hawaiian, cancer incidence and mortality, smoking and diet as factors, 0833

SUBJECT INDEX

Hispanic Health and Nutrition Survey, 0978
Hispanics in Texas, cardiovascular risk factors in children to age 18, 1464
Hispanics vs. whites, lung cancer risk, smoking as factor, 1191
Hispanics vs. whites, respiratory disease prevalence, smoking habit relationship, 1190
Japanese-American men, smoking and other factors in diabetes mellitus, 1528
Japanese males born and living in Hawaii, coronary disease risk factors, 0828
Japanese, risk factors for urothelial cancer, 0829
lung cancer incidence, vitamin A intake and smoking relationship, 0832
Maohi, French, and Chinese in Tahiti, smoking effect on lung function in adolescents, 0497
Maori in New Zealand, smoking rates compared with general population, 0404
Mormons, cancer mortality relationship to church participation, 1019
Mormons, cervical cancer incidence, 1491
Mormons vs. non-Mormons, cancer epidemiology, 1490
race-specific cancer mortality in steel plant workers, 1425
urban black adolescents, antecedents of smoking, 1225

EX-SMOKERS
(*See also* NONSMOKERS)
asymptomatic middle-aged males, small airways function, 0223
coping strategies of quitters, 6-month outcome relationship, 1377
coronary disease patients, effect on myocardial infarct and mortality, 1116
exercise program following cessation, long-term effect on abstinence, 1452
Minnesota quit smoking contest, predictive factors, 1122
pulmonary clearance in chronic bronchitis patients, 0550
recidivism predictors in males vs. females, 0655
self-quitters, determinants in abstainers vs. recidivists, 1289
self-quitters, methods and reasons in heart study participants, 1369
skills training to prevent relapse, 12-month followup, 1367
ulcerative colitis patients, efficacy of nicotine chewing gum in treatment, 1239
variables associated with cessation and maintenance, 1142

Exercise *See* **PHYSICAL ACTIVITY**

EYE DISEASES
(*See also* AMBYLOPIA, TOBACCO)
diabetic retinopathy in smokers and nonsmokers, 1557
diabetic retinopathy, smoking influence, 0239
diabetic retinopathy, tobacco chewing and cigarette smoking as risk factors, 0284
glaucoma in whites vs. blacks, risk factor study, 0999
Leber's disease and tobacco amblyopia, cyanide metabolism, 0556
pars planitis, smoking habits of patients, 1004
retinopathy, diabetes, blood pressure level, and smoking as risk factors, 1552

EYES
sensory input regulation, nicotine effects, 0031

FATTY ACIDS
(*See also* LIPIDS)
arachidonate metabolism in rats, cigarette smoke exposure effect, 0918
elastase degradation sensitivity, smoking effect, 1259
fused silica GC column for separation, 0822

FERTILITY
male subfertility, environmental risk factor survey, 0774
reduction in smokers, 0227
tobacco and alcohol use, effect in Danish women, 0161

FERTILIZATION, TOBACCO
agricultural methods to increase leaf nicotine content, 0926
burley leaf constitutents effects, 0920
chemical composition of tobacco, effect, 0823
nitrogen, effect on N-nitrosonornicotine levels, 0826
safety improvements through chemical means, 1451
slow-release nitrogen, health-related constituents, effect, 0944

FETAL GROWTH
acetylcholine-induced amino acid transport relationship, nicotine effect, 1456
intrauterine growth retardation, maternal factors and developmental effects, 0877
maternal smoking effect, 0213

FETAL MORTALITY
(*See also* INFANT MORTALITY; MORTALITY)
maternal alcohol consumption and smoking relationship, 0977

FETUS
(*See also* NEONATE; PREGNANCY)
β-endorphin and vasopressin concentrations, smoke effects, 1231
cardiovascular effects of maternal smoking, 0449
coronary arteries, maternal smoking effect on development, 0193
drug, chemical, radiation, tobacco exposure in infant glioma etiology, 1256
heart rate variability, maternal smoking effect, 0202
hemodynamics, maternal smoking effect, 0192
hypoxia, maternal smoking as factor, 1228
lung development, maternal smoking effects, 0088
maternal coffee and alcohol consumption, marijuana and cigarette smoking, effects, 1262
maternal occupational exposure to metallic mercury, reproductive effects, 0086
maternal smoking effects, 0045
maternal stress effects in women under age 18, smoking factor, 0652
pulse wave volume in descending aorta, maternal smoking effects, 0469
teratogenic effect of chronic exposure to heavy metals (cadmium) in hamsters, 1164

FIBRINOLYSIS
acute smoking effects, 0586
contraceptive hormone injections and smoke exposure in rats, effect, 0451

SUBJECT INDEX

FILTERS
carbon monoxidase for conversion of carbon monoxide in smoke, 1303
cigarettes, lung cancer risk vs. nonfiltered cigarettes, 0228
myocardial infarct and cancer epidemiology relationship, 1299
plasticizers for hardening, additives to remove harmful compounds, 0359
pressure drop of newly developed filter, 0383

FIRES
(*See also* ACCIDENTS)
tobacco industry liability in cigarette-related fires, 0843

Fluoranthenes *See* **AROMATIC HYDROCARBONS**

Forced expiratory volume tests *See* **RESPIRATORY FUNCTION TESTS**

Forced vital capacity tests *See* **RESPIRATORY FUNCTION TESTS**

FORMALDEHYDE
(*See also* ALDEHYDES)
irritant level and effect on chemosensory functioning, 0766

FUNGI
blue mold effects on terpenoids and phenolics, 0930
smoke constituent effects, 1304

GAS PHASE, CIGARETTE SMOKE
bronchial cancer formation in hamsters, carbon filter effect, 0175
lung cyclic GMP fluctuations in isolated tissues, effect, 1352
lung damage of inhaled toxins in smoke and cotton dust, 1309
mutagenic and carcinogenic compounds in Indian cigarettes, 0266
pulmonary alveolar macrophages in rats, chronic exposure effects on membrane fluidity, 0801
radicals, toxicity, 0961

GAS PHASE, TOBACCO SMOKE
mutagenic and carcinogenic compounds in Indian tobacco products, 0266

GASTRIC SECRETION
(*See also* STOMACH)
noctural vs. pentagastrin-stimulated, smoking effect, 0580

Gastric ulcer *See* **PEPTIC ULCER**

GASTROINTESTINAL DISEASES
(*See also* LIVER CIRRHOSIS; PEPTIC ULCER)
duodenal ulcer, attributable risk of cigarette smoking in males vs. females, 0650
mortality in Swedish males, smoking as factor in long-term study, 0472
ulcerative colitis patients, efficacy of nicotine chewing gum in treatment, 1239

GASTROINTESTINAL NEOPLASMS
(*See also* INTESTINAL NEOPLASMS; STOMACH NEOPLASMS)
anal cancer in women, etiologic factors, 0879
biliary tract cancer, biochemical epidemiology, 1414
diet as risk factor with alcohol consumption and smoking, long-term study, 1275
oral cancer patients, alcohol consumption and smoking as risk factors, 1182

GASTROINTESTINAL SYSTEM
(*See also* INTESTINES; STOMACH)
cadmium and nicotine, effects on digestive processes, 0628
histamine H_2-blockers, effect on gastric secretion and gastric emptying, smoking as factor, 0580
lung cancer in Billroth II resection patients, smoking as factor, 0348
nausea and abdominal discomfort with nicotine chewing gum, 0632
peptides in digestion processes, nicotine infusion effect, 0627

GENETICS, PLANTS
(*See also* HEREDITY)
burley tobacco, genetic variability to reduce tar levels, 0911
catechol and polyphenols in tobacco, genetics and breeding, 1321
insecticide effects on tobacco leaf constituents, 0948
manipulation to reduce tobacco protein, 1032
natural insect resistance development, 0805
tobacco breeding for disease resistance, 0883
tobacco inheritance patterns, breeding less hazardous leaf, 1033

Genital diseases, female *See* **GYNECOLOGIC DISEASES**

Genital neoplasms, female *See* **GYNECOLOGIC NEOPLASMS**

Gingivitis *See* **PERIODONTAL DISEASES**

Goblet cells *See* **CELLS, EPITHELIAL**

GROUP THERAPY
(*See also* CESSATION OF SMOKING, METHODS)
anger expressed by psychiatric patients, smoking prohibition effects, 1301
cessation of smoking programs, 0135
two-phase program, smoking cessation effectiveness, 0741

GYNECOLOGIC DISEASES
fertility reduction in smokers, 0227
reproductive effects of occupational exposure to metallic mercury, 0086

GYNECOLOGIC NEOPLASMS
(*See also* UROGENITAL NEOPLASMS; UTERINE NEOPLASMS)
cervical cancer, age, education, smoking as factors, screening program, 1255
cervical cancer incidence in Mormons, 1491
cervical cancer mortality, smoking relationship, 1000

HEAD AND NECK NEOPLASMS
- alcohol consumption effect on metabolism of tobacco-related carcinogens, 1347
- carcinoembryonic antigen assay in diagnosis, therapy, and followup, 1185
- inoperable patients, individualized treatment program to change destructive habits, 0785
- occupation, alcohol, and smoking as risk factors, 0070
- second primary cancer in head and neck cancer patients, smoking habit as risk factor, 0715

HEALTH EDUCATION
- (*See also* ANTISMOKING CAMPAIGNS; PREVENTION OF SMOKING; SMOKING CONTROL PROGRAMS)
- activity book on smoking and health for fourth and fifth grades, 0122
- adolescent smoking in England, analysis for video film development, 0563
- adolescents, prevention/intervention programs, 0006 1132
- adolescents in Athens, lack of knowledge of smoking-related risks, 0251
- adolescents in Italy, respiratory function tests as tool for smoking cessation, 0330
- age antismoking information was given, effects on smoking prevention, 0233
- antidrug message source credibility, 0860
- antismoking materials provided at a health fair and attempts to quit smoking, 1334
- antismoking survey and materials for health professionals, AMA program, 1366
- armed forces in Egypt, efficacy for reduction/cessation of smoking, 0173
- Biofeedback Smoking Education Program, efficacy, 0835
- cancer intervention and prevention program for high-risk community, 1387
- cardiovascular knowledge assessment in high school and college students for curriculum development, 1512
- cessation of smoking intervention program for physicians using nicotine gum, 1386
- cessation of smoking strategy, efficacy vs. self-help manual vs. monetary incentive, 0607
- children aged 10 to 12, smoking prevention program effectiveness, 0040
- children aged 3 to 5 years, stories and activities used by physicians for prevention of smoking, 1476
- children and adolescents in Manitoba, smoking survey for program planning, 0081
- children and adolescents in the Netherlands for prevention of smoking, 0398
- children and adults in Pennsylvania, health department smoking deterrence project, 1395
- community and company smoking cessation programs, efficacy with/without nicotine gum, 1166
- community-wide program to reduce heart disease, 1430
- consumption effects by social class, with cigarette tax changes, 0542
- coronary disease patients, individualized approach for smoking cessation, efficacy, 0581
- curriculum for residents in family medicine, training in patient counseling, 0761
- disease prevention and health maintenance program in a Veterans Administration Medical Center, 1536
- doctors as educational role models, 0335
- elementary and junior high schools in California, for smoking prevention/cessation, 0675
- elementary school intervention/prevention programs, 0235 1533
- emotional, ethical, physical aspects of smoking, factors in antismoking education, 0353
- employees, based on health behavior inventory, to encourage wellness, 1243
- general practitioners for smoking cessation in patients, efficacy, 0038
- Healthstyles program to promote health-enhancing behaviors, including smoking cessation, 0074
- heart disease risk reduction, efficacy of nurse intervention in a general practice, 0528
- high-risk youth, prevention of smoking efficacy, booster session effect, 1532
- hospitalized respiratory disease patients, effect of antismoking program on smoking cessation, 0130
- information kit on smoking hazards to increase smoke-free areas in workplaces, 0063
- insurance company employees following spirometry testing, 1448
- junior high school students, prevention/intervention programs, 0725
- Kaiser-Permanente risk reduction program for stress and smoking cessation, 0642
- kibbutz members by community physician, efficacy for smoking cessation, 0313
- Know Your Body program, efficacy, 0780
- Latrobe Valley (Canada) community smoking control project, 4-year evaluation, 0079
- lecture method for smoking cessation, efficacy, 0118
- Lifecycle model of preventive health services for risk factor reduction, 1242
- military enlisted personnel in Italy, cessation of smoking as program component, 0334
- Minnesota Heart Health Program for cardiovascular disease risk reduction, 1120
- mortality reduction in tobacco users who quit or reduce use, 0287
- My Body program for primary school students in England, effect on smoking onset, 0568
- myocardial infarct patients by nurses, efficacy for smoking cessation, 0599
- Napa Drug Abuse Prevention Project, evaluation of influence, 0647
- national survey of smoking and drinking behavior in Ireland to identify target groups, 0295
- North Karelia project, efficacy for smoking cessation, disease reduction, 0201
- North Karelia Youth Project, to reduce smoking and other unhealthy behaviors, 0200
- nurse's advice to quit, efficacy with/without carbon monoxide test, 0548
- pamphlet of health effects of passive smoking for health providers, 1539
- parents of newborns to reduce passive smoke exposure, 0029

SUBJECT INDEX

peer-assisted smoking prevention program for seventh grade in Canada, 0083
peer leaders for prevention of smoking in sixth graders, 1364
physician's advice, effect on cessation, 0120
prenatal care program for reduction of premature births, efficacy, 0692
preschool children, effect on behavior, attitudes, beliefs, and values, 1482
preventing or reducing causes of cancer, 1195
prevention/cessation recommendations for health authorities in England and Wales, 0553
prevention of smoking curriculum, 0127
Primary Health Curriculum Project, followup study, 1524
Project VOTE, Kansas program to promote workplace smoking policy, 0876
psychological and cognitive factors in smoking onset to develop effective programs, 0562
public information and school programs in Israel for prevention/cessation of smoking, 0304
revision of "Smoking and Health Experiments, Demonstrations, and Exhibits", 1374
school-based smoking prevention program, evaluation of two strategies, 1213
schoolchildren aged 10 to 12, efficacy for prevention of smoking, 0589
science-oriented antismoking curriculum for high school students in Israel, effect, 0311
student assemblies on health, effect on smoking cessation, 1042
students in grades 3 through 10 in Washington State, long-term smoking prevention program, 1516
technical school students, attitudes toward smoking, 0002
tobacco consumption in Greece, effect with legislation, 0253
U.S. Army program for smoking cessation, with self-hypnosis training, 1167
villages in Finland, health care personnel training effect, 0205
visual, audio, and media campaign against tobacco use, effect on oral cancer incidence, 0288
warnings in cigarette advertisements, effect of size and page placement, 0014
Washburn University health fair for antismoking education, 0880
worksite smoking cessation program, 0526

HEALTH PRACTICES
adolescents in Israel, interrelationship with smoking habit, 0305
cancer hospital employees vs. general hospital employees vs. general population, 0518
cancer patients, epidemiology data system, 1269
characteristics of smokers, nonsmokers, and ex-smokers, 0350
children and parents, education for cardiovascular risk reduction, 1411
children, Primary Health Curriculum Project, followup study, 1524
community-wide education program to reduce heart disease risk factors, 1430
head and neck cancers, risk factor with alcohol, smoking, and occupation, 0070
health behavior inventory for corporate settings to encourage employee wellness, 1243
Hispanic Health and Nutrition Survey, 0978
Know Your Body program participants, effect on knowledge, behavior, smoking initiation, 1214
National Health and Nutrition Study, 10-year followup, 0976
National Health Interview Survey, 0979
national survey, long-term health behavior patterns, England, 0560
National Survey of Family Growth, 0981
North Karelia cardiovascular disease intervention program, effect on smoking habits, 0197
physical activity as protection against myocardial infarct, smoking relationship, 0718
preschool children and parents, effect of special curriculum, 1482
prevention index, measure of health strategies and behaviors of adult Americans, 1396
psychological comparison, asbestos workers vs. mesothelioma patients vs. postal workers, 1223
self-report questionnaire, discrimination of smokers, ex-smokers, nonsmokers, 1513
social support systems, effect on disease risk behaviors including smoking, 1477
urban black adolescents, as antecedents of smoking, 1225
veterans in self-help smoking cessation program, effect on outcome, 1106
Wisconsin adults, survey, 1551

Hearing *See* **EARS**

HEART
(*See also* CARDIOVASCULAR SYSTEM)
autoregulation in response to stress, smoking relationship, 1412
size and circulatory effects of smoking in coronary disease patients, 0888

Heart disease, ischemic *See* **CORONARY DISEASE**

HEART DISEASES
(*See also* ARRHYTHMIA; CARDIOVASCULAR DISEASES; CORONARY DISEASE)
cardiomyopathy, ventricular wall motion abnormalities, smoking as factor, 1549
chronic cor pulmonale patients, bidi, hukka, and cigarettes as factors, 0275
community-wide education program to reduce risk factors, 1430
congenital, environmental risk factors including maternal smoking, 1025
coronary disease, smoking as risk factor, 1523
intervention and prevention program for high-risk community, 1387
ischemic disease in Japanese-American men with diabetes, smoking as factor, 1528
Kuopio Ischaemic Heart Disease Risk Factor Study, 0204
Minnesota Heart Health Program for reduction through community education, 1120
mortality, smoking relationship, 0564
nurse intervention for smoking cessation and risk factor reduction, efficacy, 0528
personal vulnerability, perception in light smokers vs. heavy smokers vs. ex-smokers, 1109
prediction model, heart response to hypoxic stress, 1412

risk factor intervention trial participants, 3-year followup, 1045
risk factor prevalence survey, Australia 1980, 0016
stroke mortality in Israeli heart disease study cohort, 15-year followup, 0308

HEART FUNCTION
(*See also* ARRHYTHMIA; BLOOD CIRCULATION; ELECTROCARDIOGRAPHY)
air crewmen, coronary disease risk factor determination, 1465
carbon monoxide and altitude effects in rats, 1469
cardiac electrophysiology, cigarette smoke effects, 1036
exercise capacity, smoking effect, 0640
Framingham Offspring Study, Cycle III, 1041
hemodynamics and metabolism in coronary disease patients, smoking effect, 0887
nicotine and carbon monoxide effects in smoke-exposed rabbits, 0155
nicotine and cigarette smoke effects in monkeys and cats, 0264
nicotine effects, 0210
ventricular wall motion abnormalities, smoking as factor, 1549

HEART RATE
(*See also* HEMODYNAMICS)
Biofeedback Smoking Education Program, measurement as feedback element, 0835
exercise response in smokers vs. nonsmokers, 0601
fetal, maternal smoking effect, 0202
fetal, maternal smoking effect in baboons, 1231
high arousal vs. low arousal situation smokers after first cigarette of the day, 0579
maternal smoking effects in mother and fetus, 0192
nicotine and cigarette smoke effects in monkeys and cats, 0264
nicotine effect, 0210
nicotine sensitivity marker, 0897
normotensive vs. hypertensive subjects, smoking effect, 1224
physical activity, carbon monoxide vs. smoking effects, 0169
Vitamin C and acute smoking effects, 0604

Hemagglutinins *See* ANTIBODIES

HEMODYNAMICS
(*See also* BLOOD CIRCULATION; BLOOD PRESSURE; HEART RATE)
acute smoking effects, 0586
cigarette smoke vs. methylamine vs. buffer effects, 1281
fetus, maternal smoking effect, 1228
hemoglobin concentration, hematocrit, oxygen saturation in smokers vs. nonsmokers, 0602
maternal smoking effects in mother and fetus, 0192
nicotine effect on main and digital vessels, 0842
nicotine effects in canine stomach, 1358
obese vs. nonobese elderly women, smoking effect, 0885
pathogenesis of occlusive heart disease, hemostatic variables, smoking effect, 0541
physical endurance tests, effect of smoking under normal and low atmospheric pressure, 0206
pulse rate in deprived inhalers vs. noninhalers, 0487
smokers vs. nonsmokers, 0436
vasodilator and vasoconstrictor responses in smokers vs. nonsmokers, 1484

HEMOGLOBINS
(*See also* ERYTHROCYTES)
benzo(*a*)pyrene levels, monoclonal antibodies for quantitation, 1230
birth weight relationship in healthy women who smoke during pregnancy, 0415
4-aminobiphenyl-hemoglobin adducts for estimating human exposure levels, 1077
healthy smokers vs. nonsmokers, sex and age as factors, 0602
oral leukoplakia risk relationship, 1459

Hepatic *See* LIVER

HEREDITY
brain tumors in children and adolescents, risk factor with smoking, 0733
carcinogen metabolism in liver and pancreatic cells of humans, rats, and hamsters, 1163
chronic bronchitis vs. airways obstruction, risk relationship, 1005
chronic disease mortality, effect with air pollution, smoking, and ionizing radiation, 1410
family history of coronary disease, relationship with future risk, 0420
genetic—epidemiologic characteristics of smokers vs. nonsmokers, 0998
genetic factors in nicotine tolerance in rats, 0757
lung function, age, and smoking, effect on mortality, Baltimore longitudinal study, 0997
male subfertility, factor with smoking, 0774
obstructive airways diseases, risk factors determination, 0617
pancreatic cancer, family history as factor with smoking, alcohol consumption, diet, 0036
phenotype Pi, effect on %La$_1$-antitrypsin in smokers vs. nonsmokers, 0224
twins, effect with environment on drug use, 0754

HETEROCYCLIC NITROGEN COMPOUNDS
(*See also* CARBAZOLES, INDOLES)
metabolism and mechanism of action of 7H-dibenzo(*c, g*)carbazole, 1361

HISTAMINE
(*See also* ALLERGY)
bronchial responsiveness as early indicator of airflow obstruction, 0043
bronchial tree levels, smoking effect, 0181
mediator in asthma, with leukotrienes, smoking effect, 0853
plasma levels in guinea pigs, smoke exposure effect, 0377

HORMONES
(*See also* CATECHOLAMINES)
androgen—N-nitrosodimethylamine interaction in mice, 0781
cortisol, growth hormone, and prolactin, nicotine and carbon monoxide effects, 0746
estradiol levels in infertile men, smoking effect, 1098
estradiol treatment effect on thromboxane and prostacyclin systhesis, with smoking, 0918

estrogen production by placental aromatase in rats, inhibition, 1240
estrogens, cancer and cardiovascular disease in women, risk relationship, 1078
guanylate cyclase turnover effects, 0740
opioid peptide release, nicotine effect, 1392
nicotine and benzo(*a*)pyrene, effect on normal and ectopic production, 1064
normotensive vs. hypertensive subjects, smoking effect, 1224
pituitary hormone secretion in rats, nicotine and smoke inhalation effects, 0454
progesterone and estrogens in pregnancy, smoke constituents effect on enzyme synthesis, 0392
serum prolactin, alcohol withdrawal, nicotine intake, and anxiety relationships, 1302
smoking effect on thyroid hormones, 0458
steroid, with nicotine, behavioral and motor effects in mice, 0818
testicular androgens, pubertal, smoking, and dioxin effects, 1186
testosterones and gonadotropins in young, middle-aged, and elderly men, smoking effect, 0054
urinary and serum levels in pregnant women, smokers vs. nonsmokers, 0379

Hydrogen cyanide *See* CYANIDES

HYPERCHOLESTEREMIA
(*See also* BLOOD CHOLESTEROL; BLOOD LIPIDS)
coronary disease risk relationship to educational level, 0297

HYPERLIPIDEMIA
(*See also* BLOOD LIPIDS; BLOOD CHOLESTEROL)
cardiovascular disease risk factor with smoking, treatment approaches, 1350
peripheral arterial disease in patients, cardiovascular disease prediction, 0699

Hyperlipoproteinemia *See* HYPERLIPIDEMIA

Hypersensitivity *See* ALLERGY

HYPERTENSION
(*See also* BLOOD PRESSURE)
adolescents, factors in etiology, 1444
cessation of smoking in patients, comparison of methods, 0191
coronary disease risk relationship to educational level, 0297
diabetic retinopathy relationship, 1557
health risk factor in urban areas of Shanghai, with smoking, 0145
hemodynamic and hormonal effects of smoking in hypertensives, 1224
multidisciplinary intervention program for physicians, with smoking cessation techniques, 0605
myocardial infarct in women, synergistic risk with smoking and oral contraceptive use, 1053
North Dakota telephone risk factor prevalence survey, 1338
occupational exposure to noise, relationship with smoking and other factors, 1418
population in rural Shanghai, smoking relationship, 0146
pregnant women, smoking habit relationship, 0045
sodium-dependent lithium efflux in psychiatric diagnosis, tobacco use influence, 0837
stroke risk factors in patients, with smoking, 1485

HYPNOSIS
cessation of smoking in coronary disease patients, efficacy, 1548
chewing tobacco users, efficacy for cessation treatment, 0749
individualized treatment vs. relaxation therapy for smoking cessation, 0735
reduction of smoking, effect, 1325
single treatment method for smoking cessation, efficacy, 0118
U.S. Army program for smoking cessation, 1167

HYPOXIA
arterial wall, carbon monoxide-induced, effect on arteriosclerosis etiology, 0839
fetal, maternal smoking as factor, 1228
pathophysiologic factors in alveolar hypoxia, 1138
ventilatory response in twin pairs, smokers vs. nonsmokers, 0365

IMMUNE SYSTEM
(*See also* ANTIGENS; ANTIBODIES; ANTIGEN-ANTIBODY REACTIONS)
abnormalities in asbestos workers, smoking as factor, 0429
air pollution chemicals and smoke, hypothetical effects, 1410
antibodies against antigens associated with extrinsic allergic alveolitis, smoking effect, 0585
antibody response to smoke products, smokers vs. nonsmokers, 0028
cadmium effects on responses in mice, in vivo and in vitro assays, 0687
cigarette smoke and tobacco extracts, reactions in sensitive vs. nonsensitive subjects, 0966
cigarette smoke-exposed rats, effect on antibody response, 0915
IgA in sputum and serum of surgical patients, 1333
industrial noise effects in smokers and nonsmokers, 0438
review article on effect of smoking, 0431
surgery patients who smoke, presurgery abstinence effect, 0513
T, B, macrophages, benzo(*a*)pyrene-induced changes in pregnant mice and progeny, 0820

IMMUNOGLOBULINS
(*See also* PROTEINS)
blood levels in smokers vs. nonsmokers, 0436
IgG antibodies in smokers, 0028
industrial noise effects in smokers and nonsmokers, 0438
patterns of immunoglobulin E in cigarette smokers vs. ex-smokers, 0958
saliva levels in 13-year-olds, smokers vs. nonsmokers, boys vs. girls, 0437
sarcoidosis patients, density and binding sites of IgG in monocytes, 1415
secretory component of immunoglobulin A as marker of neoplastic growth in lungs, 0768
serum IgD changes in smokers vs. ex-smokers vs. nonsmokers, 0963

SUBJECT INDEX

Incentives *See* **MOTIVATION**

INDOLES
(*See also* HETEROCYCLIC NITROGEN COMPOUNDS)
chemoprevention of nitrosamine-induced pulmonary and hepatic tissue damage, 1360

INFANT MORTALITY
(*See also* FETAL MORTALITY; MORTALITY; NEONATE)
maternal smoking relationship, 0419

Infant, newborn *See* NEONATE

INFANTS
(*See also* NEONATE)
acute otitis media with effusion, passive smoking relationship, 1324
asthma and bronchitis, lung function effects in childhood and adolescence, 0044
birth defects associated with maternal drug abuse and smoking, 1043
birth weight and mortality, maternal smoking effect, 0419
bronchiolitis, passive smoking relationship, 0023
coronary arteries, maternal smoking effect on intimal layer, 0193
glioma etiology, passive smoking as factor, 1256
low birth weight, maternal smoking effect, 0360
maternal smoking and hemoglobin levels during pregnancy, birth weight effects, 0415
maternal smoking during pregnancy, followup of long-term effects, 0162
mental and physical effects of maternal smoking, alcohol, and marijuana use, 0071
morbidity in breast- vs. formula-fed, maternal education and smoking relationship, 0878
passive smoking risk reduction, 0029
postprandial colic in 3-month-old babies, parental smoking as factor, 0225
respiratory syncytial virus infection, long-term effect, parental smoking as factor, 1287
respiratory viral infections and illnesses, parental smoking as factor, 1462

Influenza *See* **RESPIRATORY TRACT INFECTIONS**

INFORMATION SERVICES
NCI, telephone communication network for smokers who want to quit, 1307

Insecticides *See* **PESTICIDES**

INTELLECTUAL DEVELOPMENT
(*See also* COGNITION)
child at age 10, parental smoking relationship, 1192
children at 5 years of age, effect of maternal smoking during pregn 1229
children at 7 years of age, effect of maternal smoking during pregnancy, 0573
children at 3 years of age, maternal smoking effect, 1022

INTESTINES
(*See also* COLON; GASTROINTESTINAL SYSTEM)
blood flow in dogs, nicotine effect, 1357
duodenal mucosal blood flow, cigarette smoke vs. nicotine effects in rats, 0748

Irradiation *See* **RADIATION**

ISCHEMIA
(*See also* BLOOD CIRCULATION; VASCULAR DISEASES)
aluminum industry workers in Quebec, occupational exposure and smoking as risk factors, 0087
mortality, cigarette consumption relationship, 0564

Isoproterenol *See* **CATECHOLAMINES**

Keratoacanthoma *See* **SKIN NEOPLASMS**

KIDNEY DISEASES
blood nicotine levels in patients with renal failure, 1438

KIDNEY NEOPLASMS
(*See also* UROGENITAL NEOPLASMS)
genetic, occupational, and other risk factors for renal cell carcinoma, 1363
pathological factors, smoking relationship, 1060

KIDNEYS
(*See also* UROGENITAL SYSTEM)
arteriovenous fistulas used in dialysis, smoking effect on long-term patency, 0595
atherosclerosis in patients with renal failure, factors, 1534
cadmium levels in smokers and nonsmokers, 1298
heavy metal exposure, synergistic effect with smoking, 1221
hemodialysis patients, renal function impairment effect on nicotine excretion, 1433
N-nitrosodimethylamine-hydroxylase activity in mice, sex differences, 0781
nitrosamines, metabolism and hormonal regulation, 0782

LARYNGEAL NEOPLASMS
(*See also* RESPIRATORY TRACT NEOPLASMS)
alcohol and smoking, synergistic effect in etiology, 0296
alcohol consumption, occupation, smoking as risk factors, 0347
environmental factors in incidence in coastal Texas, with smoking, 1473
males in India, bidi smoking relationship, 0271
mortality, smoking relationship, 0243
occupational exposure and smoking as risk factors, 0457
women in India, snuff use relationship, 0269

Laryngitis *See* **RESPIRATORY TRACT INFECTIONS**

LARYNX
(*See also* RESPIRATORY SYSTEM)
dysplasia recurrence following treatment, smoking as factor, 0457

LEAD
(*See also* METALS, METAL ISOTOPES)
blood levels in copper smelter workers, smoking effect, 1244

environmental and industrial exposure, synergistic effect with smoking, 1221
melanosis in occupationally exposed workers, smoking as factor, 0381
pregnant women, exposure effects, with smoking and alcohol use, 1344
serum levels in cab drivers, respiratory disease relationship, 0241
soil and leaf levels on Ontario farms, 0062
tobacco grown on sludge-amended soil, levels, 1030
urinary levels in population with low exposure, smoking effect, 0056

LEARNING
(*See also* COGNITION; INTELLECTUAL DEVELOPMENT)
infant and child developmental effects of maternal tobacco, alcohol, and marijuana use, 0071

LEGISLATION
cigarette advertising ban, effects on tobacco companies' market shares, 0776
clean indoor air laws, effect on consumption, cessation, and initiation of smoking, 1166
knowledge and attitudes toward possible smoking restrictions in Ontario, Canada, 0138
nonsmokers' rights groups, impact on passive smoking regulations, 1342
prohibition of cigarette sales to minors, awareness of shopkeepers in England, 0516
restraints on smoking and cigarette promotion in New Zealand, recommendations, 0403
restriction on workplace smoking, employees' attitudes, 1351
review and critique of existing legal approaches to smoking control, 1047
tobacco consumption in Greece, effect with health education, 0253
UICC cancer prevention project, recommendations, 0003
ventilation requirements to reduce passive smoking risk, 0783
Western Australia, tobacco advertising increase during parliamentary debate, 0020

LEUKEMIA
(*See also* NEOPLASMS)
adult males, risk factors with smoking, 1474
children under 14 years of age, passive smoking as factor, 0317
epidemiology, smoking as factor, 0510

LEUKOCYTES
(*See also* BLOOD; LYMPHOCYTES)
aneurysm patients, elastolytic activity in smokers, 0630
benzo(*a*)pyrene diolepoxide-DNA adducts in exposed workers, lung cancer risk, 0982
bone marrow production in smoke-exposed mice, 0886
cholesterol-enriched diet and smoke inhalation in rabbits, effect on adhesiveness, 0372
chronic cigarette smoking effect on number and type in peripheral blood, 0908
elastolytic activity in rat lung exposed to cigarette smoke, 1117
metabolism, smoking-related changes, 0183
migration inhibition against tobacco antigens in thromboangiitis obliterans patients, 0274
nicotine effects at molecular level, 1285
nonsmokers vs. smokers, consumption level as factor, 0220
polymorphonuclear leukocytes in lavage fluid from patients with chronic airflow obstruction, 1538
umbilical veins of newborns, maternal smoking effect, 0159

LEUKOPLAKIA
(*See also* MOUTH NEOPLASMS; PRECANCEROUS CONDITIONS)
malignant potential of tobacco-induced vs. idiopathic leukoplakia, 0165
malignant transformation, tobacco use as factor, 0714
naswar (powdered tobacco) users in Pakistan, prevalence, 0425
oral, cancer development risk factors, etiology, 0262

LIPIDS
(*See also* BLOOD CHOLESTEROL; BLOOD LIPIDS; FATTY ACIDS; TRIGLYCERIDES)
atherosclerosis patients with renal failure, risk relationship, 1534
phospholipids in bronchoalveolar lavage, smokers vs. nonsmokers, 0544
reduction and improved smoke safety in flue-cured tobacco, 0804

LIPOPROTEINS
(*See also* PROTEINS)
blood levels in smokers vs. nonsmokers, 0436
cancer mortality in male MRFIT cohort, risk relationship with smoking, 1130
cessation of smoking effect on plasma levels, 0954
composition and metabolism in monkeys, oral nicotine administration effects, 1082
exercise, alcohol consumption, smoking effects in premenopausal women, 0934
low and high density, cardiovascular disease risk relationship, alcohol and smoking effect, 0700
tobacco chewers and cigarette smokers, serum high density lipoprotein cholesterol levels, 0285

Little cigars *See* **CIGARS**

LIVER
(*See also* GASTROINTESTINAL SYSTEM)
benzo(*a*)pyrene activity in rat tissues, nitration effect, 1158
benzo(*a*)pyrene, asymmetric interactions with DNA, 1102
benzo(*a*)pyrene biotransformation in isolated rabbit hepatocytes, 1315
cadmium levels in smokers and nonsmokers, 1298
carcinogen activation in isolated organ, 1027
carcinogen metabolism in human, rat, and hamster cell culture, 1163
cigarette smoke condensate mutagenicity in rats pretreated with N-acetylcysteine, 0339
DNA adducts analysis method for carcinogens, 1460
epoxide hydrolase activation of polycyclic hydrocarbons, 1157
mainstream and sidestream smoke condensates, effect on enzymatic activities in rats, 0343
nicotine disposition in rats, transport mechanisms of uptake and metabolism, 1284

nitrosamines, metabolic activation and chemoprevention by dietary indoles, 1360
nitrosamines, metabolism and hormonal regulation, 0782
1-phenylcyclohexene effect in rats, reversibility, 1340

LIVER CIRRHOSIS
(*See also* GASTROINTESTINAL DISEASES)
mutagenicity of urine of cirrhotics, 0857

LIVER NEOPLASMS
(*See also* GASTROINTESTINAL NEOPLASMS)
hepatitis infection, smoking, alcohol consumption, other risk factors, 0732

LONGEVITY
(*See also* AGE FACTORS; AGING)
men vs. women, smoking habit relationship, 1402
nonsmokers, men vs. women, 1397
percutaneous transluminal coronary angioplasty patients, smoking effect, 1423
physicians, effect of smoking, 1399
women, nonsmokers married to smokers vs. ex-smokers vs. nonsmokers, 0701

LUNG DISEASES
(*See also* ASTHMA; CHRONIC BRONCHOPULMONARY DISEASE; PNEUMOCONIOSIS; PULMONARY FIBROSIS; RESPIRATORY TRACT DISEASES)
alpha$_1$-antitrypsin phenotype relationship, smoking as factor, 1151
alveolar macrophage physiology in interstitial lung disease, 1499
asbestos-related, cancer prevention with retinol and beta-carotene in patients, 1531
asbestos workers, smoking as factor, 0429
bacterial adherence in colonization of airways, smokers vs. nonsmokers, 1249
bakers, occupational exposure, genetics, and smoking as risk factors, 0248
bronchial mucosa specimens vs. bronchial washings, value for bacteriological study, 0426
bronchoalveolar lavage in diagnosis and disease progression, 0428
C5 role in initiating influx of inflammatory cells in disease etiology, 0753
cessation of smoking for lung clinic patients, efficacy, 0179
childhood diseases in women, lung cancer risk relationship, 0731
chronic obstructive pulmonary disease, biochemical determinants, 1259
coal miners, prevalence and longitudinal changes, 15-year followup, 1545
computer-based analysis of gallium-67 uptake in normal and diseased lungs, 0103
farmers in Japan, smoking effect on serum antibodies to *Micropolysposra faeni*, 0366
passive and active smoking as risk factors in Greek women, 0255
pleural plaques in asbestos-exposed workers, smoking relationship, 1389
pneumoconiosis in coal workers, role of lung proteases and antiproteases, 1247
poultry workers, dust and bacterial endotoxin levels and smoking as factors, 0465
puffing characteristics of smokers, relationship, 0489
pulmonary surfactant, role in smoking-related diseases, 0544
red blood cell antioxidants, variations in smokers, relationship, 0759
respiratory tract glycoproteins as markers of susceptibility, 0769
sarcoidosis and pneumonia patients, smoking effect on lung defense mechanisms, 0378
sarcoidosis, lung function in smokers vs. nonsmokers, 0094
sarcoidosis, monocytes in patients, density and IgG binding sites, 1415
smoking patterns and beliefs in patients, 1558
women, lung cancer risk factor with diet and smoking, 0730

LUNG FUNCTION
(*See also* PULMONARY CLEARANCE; RESPIRATORY FUNCTION TESTS)
ABH antigens, secretor status relationship in smokers and nonsmokers, 0546
abnormal, in lung cancer etiology, with smoking, 0260
acoustic energy response to determine pulmonary system status, 0840
acute and chronic effects of cigarette smoking, 0363
adolescents, asthma and bronchitis in infancy, effect with smoking, 0044
adolescents, decline as tool for antismoking campaigns, 0226
adolescents, early smoking-induced changes, 0328
aging effects in nonsmokers, ex-smokers, and smokers, 1419
aging effects with smoking, Baltimore longitudinal mortality study, 0997
air pollution effects in India, smoking as factor, 0293
air pollution effects in smokers vs. nonsmokers, 0682
air pollution, occupational exposure, and smoking effects in Los Angeles, 0722
airway hysteresis in smoking-related chronic obstructive pulmonary disease patients, 0679
airways responsiveness in adults, smoking effect, 1096
alveolar hypoxia relationship, 1138
alveolar macrophage elastolytic activity in current smokers vs. ex-smokers, 0302
asthmatics, smoking as factor in reversible and fixed airway obstruction, 0511
asymptomatic middle-aged male smokers, longitudinal study, 0223
athletic performance tests, effect of smoking, 0206
audible sound transmission to detect small airways disease, 0965
ceruloplasmin and ferrous iron transferrin levels, relationship, 1297
cessation of smoking advice to prevent decline, efficacy, 1123
children and adolescents in Tahiti, smoking as factor, 0497
children and adolescents, influencing factors, 0222
children and adults in Los Angeles, active and passive smoking as factors, 0689
children, maternal smoking and air pollution effects, 1063
children, parental smoking association, 1105
chronic bronchitis patients, adaptation to ozone in smokers, 1024
chronic bronchitis patients, sputum production and clearance in smokers vs. ex-smokers, 0550

chronic disease intervention program, smoking cessation effect over time, 1127
clearance rate of dust in smokers vs. nonsmokers, 1076
coal miners exposed to diesel fumes, smoking effect, 1544
coal miners, smokers vs. nonsmokers, 1546
deposition and clearance of inhaled particles, developmental age as factor, 0854
enzyme activity in smokers vs. nonsmokers, 0107
exercise capacity, smoking effect, 0640
firemen, effect of occupational exposure to smoke and smoking, 0509
genetic—epidemiologic differences, smokers vs. nonsmokers, 0998
health fair testing, antismoking tool at Washburn University, 0880
healthy smokers, transit time analysis of forced expiration after H_2O mist exposure, 0329
high- vs. low-tar cigarettes, inhalation pattern change, effect, 0792
Hispanics vs. whites, smoking habit relationship, 1190
inflammatory effects of toxins in cotton dust and cigarette smoke, 1309
iron miners, changes over 5 years in smokers vs. nonsmokers, 0221
medical students aged 19 to 25, effects of age, environmental conditions, smoking habits, 0166
metoprolol and propranolol effects, 0621
mineral content in smokers with pulmonary fibrosis, effects, 1498
molecular and cellular blood components and pulmonary status, smoking relationship, 1259
neon vs. air inhalation effects, 0633
nicotine injection and smoke inhalation effects in cats and monkeys, 0265
nitrogen dioxide and ozone, long-term effects in monkeys, 0653
nonsmokers exposed to moderate and heavy cigarette smoke, influence of suggestibility, 0126
nonsmokers vs. asymptomatic smokers, epithelial alveolar permeability, 0060
Normative Aging Study in middle-aged men, longitudinal effects, 1046
obstructive disease, pathophysiological mechanisms, smokers vs. nonsmokers, 0619
obstructive disease patients, effect of smoking cessation on decline, 0622
passive smoking effects, 0018
peripheral airways obstruction as predictor of loss, sex and smoking as factors, 0105
peripheral blood leukocytes and enzyme activities, chronic smoking effect, 0908
Pi MZ heterozygous vs. Pi M subjects, smoking as risk factor, 1151
plasma protein and immunoglobulin levels in smokers, relationship, 0907
polymorphonuclear leukocytes in lavage fluid, correlation, 1538
poultry workers, dust exposure, bacterial endotoxin levels, smoking association, 0465
pulmonary metabolism of arachidonic acid, smoke inhalation effect in rats and hamsters, 0214
pulmonary tissue response to long-term smoke inhalation in young and old mice, 0895
randomly selected population in Cracow, changes over 13 years, 0434
reduced minute ventilation in animals exposed to cigarette smoke, 0479
reverse (chutta) smoking effects, 0276
sarcoidosis patients, smoking effect, 0094
second and fifth grade students, smoking and air pollution effects, 0723
simple spirometry for evaluating changes in smokers, 0279
smoke exposure effects in rabbits, 0620
smoking cessation program effects, 1300
socioeconomic status, illness, nutrition, and smoking effects in Indian adults, 0292
subjective and objective measurement of smoke inhalation, relationship in smokers, 0791
sulfur dioxide-exposed workers, smoking as factor, 1061
synergistic effect of cigarette smoke and silica dust exposure, 0475
thermoelectrical plant workers, changes over 4 years, smoking as factor, 0333
tidal carbon monoxide boost in deprived inhalers vs. noninhalers, 0487
Vitamin C and acute smoking effects, 0604
vocational school students, smokers vs. nonsmokers, 0188

LUNG NEOPLASMS
(*See also* BRONCHIAL NEOPLASMS; CARCINOMA, BRONCHOGENIC; CARCINOMA, EPIDERMOID; RESPIRATORY TRACT NEOPLASMS)
abnormal lung function, respiratory damage, and smoking as risk factors, 0260
adenocarcinoma and squamous cell carcinoma in women, risk factors, 0731
age, sex, histological type, symptoms, smoking as factors in growth rate, 0319
air pollution and smoking as risk factors, 0187
airways obstruction as risk factor, 1006
alcohol and smoking in etiology, 0296
alcohol consumption, occupation, smoking as risk factors in Poland, 0432
aromatic hydrocarbon injections in mice as inducers, 0717
asbestos workers, smoking relationship, 0565
atypical bronchial epithelial cells in sputum as markers for people at risk, 1461
benzo(*a*)pyrene-DNA binding in etiology, 1227
benzo(*a*)pyrene-induced in rats, enzyme metabolizing activity in etiology, 0872
beta-carotene and vitamin E for prevention, U.S.-Finnish efficacy trial, 0986
beta-glucuronidase in tumorigenesis in mice, 1354
Billroth II resection patients, smoking as factor, 0348
biochemical risk factors, determination in cigarette-smoking baboons, 1467
blood test as screening tool for early detection, 0116
California physicians, cessation of smoking relationship, 0685
carotene in the diet as protection, interactive effect with tobacco use, 1276
cessation of smoking program for patients to qualify for clinic treatment, 0179
chloromethyl ether-exposed workers, smoking relationship, 1388

SUBJECT INDEX

cytotoxic cell function in carcinogenesis, 0964
dark tobacco use relationship in Cuba, survey, 0985
diet, alcohol consumption, tobacco use as risk factors, long-term study, 1275
diet and smoking as risk factors in women, 0326
environmental and occupational factors, with tobacco use, 0988
environmental factors in incidence in coastal Texas, with smoking, 1473
female nonsmokers, passive smoking, air pollution, diet as risk factors, 0256
females in Hong Kong, risk factors, 0257-0259
geographical correlation with upper respiratory tract cancer in European countries, 0244
high-risk populations, risk factor determination, 0989
Hispanics vs. whites, risk factors, smoking relationship, 1191
hospitalized patients, smoking, occupation, and residence relationship, 0519
incidence rates in three Israeli towns, smoking and occupational exposure as factors, 0307
individual susceptibility in cigarette smokers, 0042
inoperable patients, individualized treatment program to change destructive habits, 0785
interferon induction in patients vs. controls vs. newborns, 0609
international collaborative study of risk factors, 0228
Italian males, occupation and smoking as risk factors, 0327
lifetime tobacco consumption correlation with incidence, 1037
males and females in Shanghai, smoking-related risk, 0142
method of smoking as risk factor in Bangladesh, 0051
miners in Canada, occupational exposure and smoking as risk factors, 0097
mortality, air pollution and smoking as factors, 0352
mortality, effect of reduced tar intake, 0039
mortality in Amish vs. non-Amish populations, nonsmoking as factor, 1398
mortality in Italy since 1955, trends, 0331
mortality in Switzerland, sex-related trends, 0495
mortality in western Scotland, passive smoking as factor, 0591
mortality, smoking as factor, 0186
Nebraska Laboratory Cancer Research Center, research objectives, 1154
nutrition, alcohol consumption, family history, occupational exposure as factors, 0034
nutrition, occupation, residence, and smoking as risk factors, 0960
occupation and smoking as risk factors, 0470
oral cancer patients, alcohol consumption and smoking as risk factors, 1182
passive smoking and occupation as risk factors in nonsmokers, 1295
passive smoking risk in nonsmoking wives of smokers, 0254
plutonium workers, smoking relationship, 1187
radon daughter and smoke exposures of uranium miners, effect on etiology, 0656
residency location and type, effect with smoking on etiology, 0453
retinol vs. beta-carotene for prevention in high-risk smokers, pilot study, 1517
screening and treatment of high-risk men, effectiveness, 1241
screening of workers at high risk for detection/prevention, 0635
sex differences in development and growth, smoking relationship, 0349
small cell, squamous cell, large cell, adenocarcinoma, smoking-related risk, 0355
socioeconomic and occupational risk factors with smoking, 1375
sputum cytology for early detection in asymptomatic smokers, 0462
tar content of cigarette smoke, influence on risk, 1216
tar content of cigarettes, effect on relative risk, 0050
tobacco smoke components, effect on pulmonary alveolar macrophages in etiology, 0803
tuberculosis patients given isoniazid, risk with smoking, 0508
UICC worldwide prevention program, 0003
uranium miners, radiation and smoking as risk factors, 1350
uranium miners, radon daughter—smoking interaction, 1492
viral transformation of fibroblasts, feasibility for susceptibility testing, 0800
vitamin A intake and smoking, relationship to incidence, 0832
western Scotland, smoking relationship, 0590
women, diet, smoking, passive smoking, vitamin A as factors, 0730
women in India, snuff use relationhip, 0269
women in Sweden, risk factors in nonsmokers, 0459
women, smoking relationship, 0090

LUNGS
(*See also* RESPIRATORY SYSTEM)
activation/deactivation of cigarette smoke mutagens by homogenized tissue, 0337
aerosol particle distribution in smokers vs. nonsmokers, 1260
alpha-1-proteinase inhibitor::elastase balance, smoking effect, 1407
alpha radioactivity of cigarette smoke filtrates, potential damage, 0865
alveolar macrophages, morphologic and functional characteristics in smokers vs. nonsmokers, 0802
arachidonic acid metabolism in smoke-exposed rats, 0890
aromatic hydrocarbons in cancer induction in mice, 0717
benzo(*a*)pyrene activity in rat tissues, nitration effect, 1158
benzo(*a*)pyrene metabolism, alcohol consumption effect, 1347
biochemistry of proteoglycans, cigarette smoking effect in baboons, 0962
carcinogen activation in isolated organ, 1027
cigarette smoke condensate mutagenicity in rats pretreated with N-acetylcysteine, 0339
computer-based analysis of gallium-67 uptake in normal and diseased lungs, 0103
cyclic GMP fluctuations, gas phase cigarette smoke effects, 1352
cytolytic functions of pulmonary effector cells, smoke inhalation effect in mice, 0903
defense mechanisms in smokers vs. nonsmokers, 0378
elastase and myeloperoxidase release in smokers as factor in emphysema development, 0919
emphysematous changes in rats, porcine pancreatic elastase and cigarette smoke relationship, 0900
epithelial cells, sensitivity to cadmium, 1121
epithelial hyperplasia and metaplasia in hamsters, effect of asbestos and BaP, 0358
high-fat diet and smoke effects on epithelial morphology in monkeys, 0868

SUBJECT INDEX

histamine and leukotrienes, site of action and mediation of asthma, smoking effect, 0853
immunoregulatory T-cells in lavage fluid, abnormalities in smokers, 0180
interleukin-1 production by macrophages, response to infection and smoking, 1165
lesion development in monkeys, effect of nitrogen dioxide and ozone, 0653
mainstream and sidestream smoke condensates, effect on enzymatic activites in rats, 0343
maternal smoking effects on fetal lung development, 0088
neonates of smoke-exposed rats, cellular and subcellular effects, 0778
neuroendocrine cell innervation in neonates of smoke-exposed hamsters, 1555
neutrophil elastase in emphysema etiology, α_1-proteinase inhibitor role, 1048
nitrosamines, metabolic activation and chemoprevention by dietary indoles, 1360
oxidative metabolism of nicotine in animal and human tissues, 0708
particle deposition during cigarette smoking, 0136
permeability in smoke- and elastase/smoke-exposed hamsters, 1119
plutonium inhalation, clearance in smoke- vs. sham-exposed rats and dogs, 1515
polonium-210 distribution and clearance of radioactivity in smoke-exposed rats, 1261
pressure-volume curves in excised rat lungs, tobacco smoke effects, 0544
pulmonary alveolar macrophages, chronic tobacco smoke exposure effects in rats, 0801
pulmonary macrophages in young and old mice, smoke exposure effects, 0896
secretory component of immunoglobulin A as marker of neoplastic growth, 0768
spicules in smoke-exposed rats, structure, interrelationships, chemical identity, 1343
sputum analysis for atypias in high-risk smokers, 0764
structure and function in obstructive airways disease, 0619
tobacco smoke constituents, deposition sites, 0506

LYMPHOCYTES
(*See also* LEUKOCYTES)
H^3-thymidine uptake against tobacco antigens in thromboangiitis obliterans patients, 0274
immunoregulatory imbalances in smokers, 0180
lung lavage fluids in disease detection, factor, 0428
lungs of young and old mice, response to long-term smoke inhalation, 0895
mitogenic response in smoke-exposed macaques and controls, 1446
nicotine effects at molecular level, 1285
sister chromatid exchanges in occupationally exposed workers, smoking effect, 0177
sister chromatid exchanges in oral tobacco users, 1489

MACROPHAGES
(*See also* CELLS; PULMONARY ALVEOLAR MACROPHAGES)
alveolar macrophage transglutaminase, inhibition by smoke, 1280
arachidonate metabolism, smoke exposure effect, 0918
bone marrow production in smoke-exposed mice, 0886
fibrotic lung disease, clinical and pathophysiological relationship, 1499
lung lavage fluids in disease detection, factor, 0428
pathogenesis of emphysema, significance of elastolytic activity, 1117
respiratory system of smoke-exposed dogs, emphysema relationship, 1179

MAMMARY NEOPLASMS
Depo-Provera use in patients in Costa Rica, smoking as factor, 0811
hair dye use and smoking as risk factors, 0341
incidence in Norway, prospective study, 0417
mastectomy patients, secondary tumors and mortality, radiation and other factors, 1067
screening with/without mammography for detection, efficacy, 0123
smoking-related risk, 0812
women in Milan, smoking relationship, 0332
women under age 50, lack of risk relationship with smoking, 1039

MARIJUANA SMOKING
adolescent male use, father's influence, 1245
adolescents and adults, typography and dose regulation, 0706
adolescents, attitudes and behavior of family, siblings, peers as factors, 1134
adolescents, effect of peer-led intervention program, 1233
adolescents, evaluation of intervention strategies, 0727
adolescents, parental, sibling, and peer influences, 1246
adolescents, prevention program, efficacy of parental involvement, 0728
childhood and adolescent use, determinant of future drug abuse, 1248
childhood and adolescent emotional and adjustment characteristics as predictors, 1393
drug abuse research, initiating and maintenance factors, 0991
high school students, related administrative problems, with alcohol consumption and smoking, 0648
morbidity and mortality relationship in Barbados, 0053
paternal influence on daughter's use, smoking relationship, 1222
pregnant adolescents, independent and dependent behavioral factors, 0657
pregnant women, effects, 0071
seventh graders, parental involvement in prevention program, effect on intentions, 0726

MARIJUANA SMOKING
adolescents, relationship with temperament in young adulthood, 1394

MASS MEDIA
antismoking articles in Israeli kibbutz newspaper, efficacy for smoking cessation, 0313
antismoking campaign for adolescents, comparison of varied program content, 1323
Australian "Quit For Life" campaign, efficacy, 0009
behavior modification clinic for smoking cessation, reinforcement campaign, efficacy, 1505

SUBJECT INDEX

- cigarette advertising in *Time* magazine 1944-1983, health claims and images, 0845
- cigarette advertising in magazines, effect on adolescents' brand preferences, 0695
- classroom television program for prevention/cessation of smoking in junior high students, 0724
- health warnings on magazine cigarette advertisments, effect of size and page placement, 0014
- microcomputer-assisted relaxation program, smoking cessation component, 1075
- pilot community smoking cessation campaign in South Australia, effectiveness, 0024
- prevention/cessation of smoking intervention programs in southwest Texas, evaluation, 1481
- prevention/cessation segment on news program, efficacy as component for seventh graders, 0725
- prevention of smoking program for fifth to seventh graders, with school health education, 1503
- television series for smoking cessation, 0198
- women's magazines in Canada, tobacco advertising vs. antismoking articles, 0090

MATERNAL-FETAL EXCHANGE
- nicotine effect on blood flow and embryo development in rats, 1111

MATERNAL SMOKING
(*See also* PARENTAL SMOKING; SMOKING)
- abortion and other factors, effect on subsequent pregnancies, 0772
- before and during pregnancy, 1978-1979 vs. 1980-1982 in Canada, 0072
- before, during, and 1 year postpartum, changes, 0073
- birth defects relationship, with drug abuse, 1043
- blood vessels in umbilical cords, effects, 0184
- bronchiolitis in infants, relationship, 0023
- cancer risk relationship in adult offspring, 1313
- developmental effects in children, 1022
- fetal activity and response to hypoxia during development in smoking baboons, 1231
- fetal and childhood development, effects, 0573
- fetal and neonatal effect, with age, alcohol consumption, socioeconomic status, 0045 1222 %
- fetal cardiovascular, respiratory, and biochemical responses, 1228
- fetal growth retardation, mechanism for effect, 0379
- fetal hemodynamic effects, 0192
- fetal lung effects, consumption level relationship, 0088
- fetal mortality relationship, 0977
- health-related risks for mother and fetus, 0808
- hemoglobin levels and birth weight relationship, 0415
- individualized counseling during obstetric care for cessation, 1504
- infant and child mental and physical developmental effects, 0071
- infant morbidity relationship in breast- vs. formula-fed, 0878
- infant pneumonia, risk relationship, 1462
- intimal layer of infant's coronary arteries, effect, 0193
- lactation and infant growth effects, with diet and alcohol use, 1525
- long-term effects on infants, 0162
- low birth weight and infant mortality relationship, 0419
- low birth weight relationship, 0360
- lung function effects in children, 1063
- mitochondrial proliferation in umbilical arteries of newborns, 0171
- National Survey of Family Growth, 0981
- neonatal effects, 0117
- O_2 transport in pregnancy at high altitudes, effects, 0755
- placental benzo(*a*)pyrene-DNA adducts, effect, 0216
- placental detoxification systems, response, 0758
- placental oxidase activities, inductive stimulus, 1346
- pregnancy outcome effects, with alcohol consumption, 1266
- preterm delivery and premature rupture of membranes, risk relationship, 0809
- prostacyclin and fibronectin production in cultured umbilical vein cells, effect, 0322
- spontaneous abortion and karyotype of abortus, relationship, 1257
- trends among pregnant women in France, 1972-1981, 0238
- umbilical arteries and veins, inhibitory effect on amino acid uptake, 1455
- unbilical and maternal blood leukocyte count, effect, 0159
- ureaplasmas, colonization in placenta, neonatal effects, 1051
- urine cotinine levels in neonates as exposure indicator, 1327

MATHEMATICAL MODELS
(*See also* STATISTICAL ANALYSIS)
- health decisionmaking in coronary artery disease patients, 1496
- lung disease patients, smoking cessation prediction, 0133
- moisture diffusion during tobacco curing, 0925

Medical students *See* **STUDENTS**

MEMORY
(*See also* COGNITION)
- health warnings on magazine cigarette advertisements, effect of size and page placement, 0014

Mental disorders *See* **PSYCHIATRIC DISORDERS**

Mesmerism *See* **HYPNOSIS**

MESOTHELIOMA
(*See also* NEOPLASMS; PRECANCEROUS CONDITIONS)
- asbestos exposure, smoking, and other risk factors, 0318
- psychological comparison of patients with asbestos workers, 1223

METALS, METAL ISOTOPES
(*See also* CADMIUM; LEAD; NICKEL; POLONIUM-210)
- carcinogenicity and bioassay screening systems, 1258
- carcinogenicity in tissue culture, 1483
- environmental and industrial exposure, synergistic effect of smoking on body burden, 1221
- hypertension, factors in etiology, 1444
- metallic mercury, reproductive effects of occupational exposure in women, 0086
- plutonium, cancer and disease risk in exposed workers, smoking effect, 1187
- plutonium levels in tobacco grown near chemical plant, potential dose, 1443
- plutonium in respiratory tracts of rats and dogs, smoke inhalation effect, 1515

selenium, cadmium, beryllium content of tobacco, biological implications, 0751
soil and leaf levels on Ontario farms, 0062
tobacco grown on sludge-amended soil, levels, 1030
zinc supplements for smokers to counteract cadmium intake effects, 1236

METHYLCHOLANTHRENE
(*See also* AROMATIC HYDROCARBONS; CARCINOGENS)
aryl hydrocarbon hydroxylase inducement in mice, effect, 0430
cytochrome P-450 induction by 3-methylcholanthrene in rats, 0990

Miscarriage *See* **ABORTION**

MOISTURE CONTENT
leaf moisture diffusion and chemical changes during curing, 0925

MORBIDITY
age, social class, and smoking relationship, 0543
air pollution effects in smokers vs. nonsmokers, 0682
alcohol consumption, smoking, and injuries as factors, Washington State survey, 1540
attribution to smoking in school-based prevention program, with skills training, 1550
blue collar workers, disease epidemiology, smoking effect, 1543
breast- vs. formula-fed infants, maternal education and smoking habit relationship, 0878
British soldiers 1959-1971, smoking relationship, 0539
cancer epidemiology in Utah, 1490
cardiovascular disease, smoking and other factors, 0700
cardiovascular, pulmonary risks related to tobacco consumption, 0168
children, maternal smoking during pregnancy effects, 1022
current and ex-smokers in Canada vs. nonsmokers, 0067
disease patterns in smokers vs. nonsmokers, 1402
doctors in Sudan, incidence of smoking-related diseases, 0448
economic costs of smoking-related illnesses in Finland, 0199
Finnish Twin Cohort Study, 6-year followup, 0203
genetic—epidemiologic differences, risks in smokers vs. nonsmokers, 0998
health effects of smoking products with reduced toxic constituents, 0641
hospital patients in Barbados, smoking relationship, 0053
MONICA project, West Germany, monitoring cardiovascular disease, 0176
myocardial infarct and angina patients, long-term effects of pipe and cigar smoking, 0301
myocardial infarct patients, long-term followup of smoking cessation effect, 0300
patients with smoking-related diseases, efficacy of multicomponent cessation program, 0849
plant workers in Czechoslovakia, cost benefits analysis in smokers vs. nonsmokers, 0153
respiratory illness in India, air pollution and smoking as factors, 0293
smoking-related in the United States, 0810
social support systems of two communities, effect on risk factors including smoking, 1477
surgery patients who smoke, presurgery abstinence as factor, 0513
tobacco consumption, price, and self-reported use, relationship, 0080
tobacco factory workers, dust exposure relationship, 0167
women, oral contraceptive use and smoking as risk factors, 0549

MORTALITY
(*See also* FETAL MORTALITY; INFANT MORTALITY)
alcohol consumption, smoking, and injuries as factors, Washington State survey, 1540
all causes in Canada, tobacco use as risk factor, 0067
analyses of risk factors, American Cancer Society, 1195
asbestos workers, smoking relationship, 0515
bladder cancer patients, secondary cancers as cause, smoking effect, 0540
California physicians, cessation of smoking relationship, 0685
cancer and heart disease in middle-aged men in Sweden, smoking and other risk factors, 0474
cancer and other diseases in Shanghai, smoking and air pollution as risk factors, 0143
cancer, cardiovascular, respiratory, and all causes, smoking-related 1980, 0971
cancer, Hawaiian ethnic groups, diet and smoking relationship, 0833
cancer in uranium miners, radon exposure and smoking as risk factors, 0242
cancer in women in Norway, prospective study, 0417
cancer, men in MRFIT, diet, vitamin A, beta-carotene, retinol as factors, 1130
cancer mortality in Poland, demographic and epidemiologic factors, 0433
cancer rates in California Mormons, lifestyle factors, 0684
cancer, risk factors determination, 0231
cardiovascular disease and cancer in women, smoking habit relationship, 1000
cardiovascular disease in Scotland, risk factor survey, 0582
cardiovascular disease, MONICA project, West Germany, monitoring, 0176
cardiovascular disease, smoking and other factors, 0700
cardiovascular diseases, peripheral arterial disease in risk prediction, 0699
chronic diseases, air pollution, ionizing radiation, smoking as factors, 1410
chronic nonspecific respiratory disease, 13-year followup, 0434
coronary disease and second primary malignancies in breast cancer patients, factors, 1067
coronary disease and all causes, 0203
coronary disease, cessation of smoking effect, 0201
coronary disease in Swedish males, intervention trial effects, 0473
coronary disease, risk factors, 0420
disease patterns and sex differences, smoking related, 1402
fetal, maternal alcohol consumption and smoking relationship, 0977
hospital patients, smoking relationship, 0053
incidence and causes in persons living with smokers, 1314
industrial workers, smoking relationship, 10-year followup, 0303
ischemic heart disease and esophageal cancer, cigarette consumption relationship, 0564
large bowel cancer, diet, alcohol consumption, tobacco use as risk factors, 0033

lung and upper respiratory tract cancers in Europe, smoking as major risk factor, 0244
lung cancer and other tobacco-related cancers in Italy since 1955, trends, 0331
lung cancer in Amish vs. Non-Amish populations, nonsmoking as factor, 1398
lung cancer in Bangladesh, effect of smoking methods, 0051
lung cancer in Switzerland, sex and age as factors, 0495
lung cancer in western Scotland, passive smoking as factor, 0591
lung cancer, projections related to tobacco consumption, 0039
lung cancer, risk factors other than smoking, 1375
lung cancer, screening and treatment of high-risk men, effect, 1241
lung cancer, smoking as factor, 0090 1472
lung function, age, and smoking effects, Baltimore longitudinal study, 0997
major causes in Shanghai, risk factor survey in urban and rural areas, 0145
middle-aged men in Multiple Risk Factor Intervention Trial, risk factors, 1128
miners in Canada, occupational exposure and smoking as factors, 0097
Mormon cancer patients, level of church participation relationship, 1019
myocardial infarct and angina patients, tobacco use relationship, 0298
myocardial infarct patient, long-term followup of smoking cessation effect, 0300
myocardial infarct patients, cigarette type as factor, 0547
North Karelia cardiovascular disease intervention program, effect on smoking, 0197
occupational and other risk factors in steel plant workers, 1425
oral cancer in rural India, tobacco use relationship, 0286
oral cavity and laryngeal cancer, smoking as risk factor, 0243
overall risk of smoking in older men and women, Denmark, 0168
percutaneous transluminal coronary angioplasty patients, smoking effect, 1423
physician's responsibility to certify tobacco use relationship, 0975
physicians, smoking relationship, 0390
psychiatric patients, smoking relationship, 0388
reduction in tobacco users who quit or reduce use, 0287
respiratory cancer and heart disease, smoking relationship, 1278
saltpeter workers, effect of asbestos exposure and smoking, 0413
smokers of less hazardous cigarettes, 0641
smoking-related in the United States, 0810
tobacco habit form in India, risk relationship, 0289
uranium miners, radiation and smoking as risk factors, 1189
veterans of World War I, smoking as factor in lung cancer and other diseases, 1011
women, oral contraceptive use and smoking as risk factors, 0549

MOTIVATION
(*See also* ATTITUDES; BEHAVIOR, HUMAN)
adolescents, developmental epidemiological studies of substance abuse, 0995
adolescents, health education for smoking cessation, respiratory function tests as tools, 0330
adolescents, value approach as coping strategy for nonsmokers, 1541
baseline characteristic predictive of success in smoking cessation, 0038
cessation of smoking, reason given for dropping out of program, 0209
cessation of smoking success, importance, 0219
current vs. ex-smokers to smoke, differences, 0552
desire to quit as predictor of the decision to stop smoking, 1335
followup letters to motivate and maintain smoking abstinence, 1337
health locus of control and self-efficacy, factors in cessation success, 1457
heavy smokers, psychological characteristics as factors, 0501
hypnosis cessation of smoking treatment, importance for success, 0680
nurses, attitudes and factors in smoking cessation, 0773
partner support/participation in skills training smoking cessation program, efficacy, 1379
persuasive communication to bolster intentions and confidence in smoking cessation, 0524
predictors for cessation in addicted smokers, nicotine gum effects, 0683
pregnant women, effect on cessation of smoking, self-help vs. group therapy, 0646
pulmonary disease patients, motivation to quit smoking, 1558
sedative vs. stimulant smokers, perceived stress and arousal as factors in behavior, 0561
self-help smoking cessation, stages of change prediction, 1434
self-help smoking cessation, successful quitters vs. recidivists, 1065
tobacco and alcohol intervention program for under-25-year-olds, factor, 0659
tobacco use in psychiatric patients, motivational factors, 0098
videotapes at workplaces for smoking cessation, effect, 0504

MOUTH
(*See also* GASTROINTESTINAL SYSTEM)
gingival epithelium ultrastructure in smokers' melanosis, 0461
oral pigmentation in smokers vs. nonsmokers, 0314
tobacco-related carcinogens, alcohol consumption effect on metabolism, 1347

MOUTH DISEASES
(*See also* GASTROINTESTINAL DISEASES)
leukoplakia, malignant potential of tobacco-induced vs. idiopathic, 0165
melanosis, incidence in lead workers vs. smokers, 0381
oral lichen planus lesions, smoking effect on malignancy development, 0163
submucous fibrosis, betel nut chewing as risk factor in South African Indians, 0446
ulcers following smoking cessation, 0026

MOUTH MUCOSA
benzo(*a*)pyrene, β-naphthylamine activation by epithelial cells, 0158
beta-carotene and retinol deficiency in heavy smokers and alcohol consumers, 0066
buccal pouch tumors in hamsters, anticarcinogenic activity of vitamin E, 1059

keratin expression in cultured cells, tobacco smoke condensate effects, 0157
melanin pigmentation in smokers vs. nonsmokers, 0476
naswar (powdered tobacco) use in Pakistan, effects, 0425
oral tobacco use effects, 1489
permeability to nitrosonornicotine, with/without ethanol, 0875
smokeless tobacco and snuff, effects in hamsters, 1058
tobacco and betel nut extracts, effects in hamster cheek pouch, 0498

MOUTH NEOPLASMS
(*See also* GASTROINTESTINAL NEOPLASMS; LEUKOPLAKIA)
added risks in patients who continue to smoke, 0702
aerodigestive and lung primary cancers in patients, alcohol consumption and smoking as risk factors, 1182
alcohol consumption and smoking as risk factors, 0345
alcohol consumption and smoking relationship, Israel vs. United States, 1282
alcohol consumption effect in smokers and hamsters, use level relationship, 1253
alcohol consumption in nonsmokers, risk relationship, 1183
biochemical indicators of carcinogenesis, smoking as factor, 1184
buccal pouch tumors in hamsters, anticarcinogenic activity of vitamin E, 1059
diet, alcohol consumption, tobacco use as factors, 0032
etiology, tobacco and other environmental factors, 0858
gamma-glutamyltranspeptidase role in etiology, with smoking, alcohol consumption, aging, 0841
health education campaign against tobacco use, effect on incidence, 0288
high-risk populations, risk factor determination, 0989
leukoplakia malignant transformation, tobacco use as factor, 0714
levels of IgA and its secretary component in patients, 1333
mortality risk in rural India, tobacco use relationship, 0286
mortality, smoking relationship, 0243
mouthwash, alcohol use, and smoking as factors, 1216
naswar, powdered tobacco used in Pakistan as risk factor, 0425
N-nitrosamine formation in areca chewers, relationship, 1196
oral lesions carcinogenesis, smoking relationship, 0163
oral leukoplakia patients, risk and etiology, 0262
palate and tongue cancer in reverse smokers, beta-carotene as preventive treatment, 0065
reverse smoking and smoking relationship in Colombia, 0150
screening project for smokers over age 40, 0938
snuff and chewing tobacco use, relationship, 0988
submucous fibrosis and oral cancer in South Africa, betel chewing as factor, 0446
tobacco chewing as risk factor, 0272
tobacco smoke as causative factor, data analysis for European countries, 0244
x-ray exposure, smoking, and other factors in etiology, 0721

MUSCLES
airway smooth muscle, nicotine effect on leukotriene D_4-induced responses, 1153
muscle tension and effectiveness of followup letters to maintain smoking abstinence, 1337
smooth muscle cells, physiological effects of nicotine, 1093
snuff-dipping and tobacco chewing, effects, 1463
stretch receptors in crayfish, nicotine chemosensitivity, 0892

MUTAGENESIS
benzo(*a*)pyrene, binding of metabolites to DNA, 1449
cigarette smoke condensate and benzo(*a*)pyrene, antimutagenic compounds, 0394
cigarette smoke condensate and norharman, co-mutagenic activity, 0395
cigarette smoke effect on activation/deactivation of mutagens in human lung preparations, 0337
condensate level and nicotine level relationship, 1304
gynecologic neoplasms, mutagenicity of cervical fluid in smokers, factor, 0711
7H-dibenzo(*c, g*)carbazole and metabolites in whole-cell system, 1361
sister chromatid exchanges, induction by cigarette condensates, 0195
tobacco pyrolysates in rat lung, alcohol consumption effects, 1293

MUTAGENS
absorption from crude coal tar in psoriasis patients, 0743
cigarette smoke condensate, effect of thiols on activation in Ames test, 0339
excretion in urine of smokers and cirrhotics, 0857
indirect, co-mutagenic effect with cigarette smoke condensate and norharman, 0395
marijuana and tobacco smoke condensates, chemical/biological analysis, 1320
sputum levels in occupationally exposed workers, smokers vs. nonsmokers, 0422
tobacco flavor compounds in low-tar cigarettes, 1198
urine level in railroad workers, smoking effect, 0677
urine levels in industrial workers and nurses, smoking effect, 0402

MYOCARDIAL INFARCT
(*See also* CORONARY DISEASE)
cessation of smoking in patients, long-term effects on morbidity, mortality, 0300
Chinese patients in Shanghai, smoking relationship, 0147
coronary disease patients, effect of smoking cessation, 1116
etiology, tobacco and other environmental factors, 0858
health education of patients by nurses, efficacy for smoking cessation, 0599
international project to monitor trends and determinants of cardiovascular diseases, 0059
international study of infarct survival, cigarette type as factor, 0547
men under 55 years of age, smoking effect on risk, 1040
middle-aged men, rehabilitation program effect on prognosis, smoking reduction, 0399
nurses, risk in smokers vs. never smokers, 1054
physical activity as protection, smoking relationship, 0718
pipe and cigar smoking by patients, long-term effects, 0301
platelet aggregation alteration, influence of smoking diabetes, sex, 0608
psychosocial and demographic factors related to cessation of smoking in patients, 1086

- rehabilitation program for patients, smoking as psychosocial factor, 0152
- risk associated with less hazardous cigarettes, 1299
- short-term prognosis in smokers, 0298
- videocassette smoking cessation program for recovering patients, efficacy, 0654
- women, incidence in smokers vs. nonsmokers, Framingham study participants, 0987
- women, smoking as risk factor, 0464

Naphthalenes *See* **AROMATIC HYDROCARBONS**

Naphthylamines *See* **AROMATIC AMINES**

NASAL MUCOSA
- N'-nitrosonornicotine activity in rats, alcohol consumption effect, 1204

NASOPHARYNGEAL NEOPLASMS
(*See also* PHARYNGEAL NEOPLASMS)
- occupational exposures, risk with smoking and alcohol consumption, 0720

Nass chewing *See* **TOBACCO CHEWING**

Neck neoplasms *See* **HEAD AND NECK NEOPLASMS**

NEONATE
- birth weight, maternal smoking effect, 0573
- blood vessels in umbilical cords, maternal smoking effects, 0184
- cellular and subcellular effects of maternal smoke exposure, 0778
- growth and behavior, maternal smoking effects, 1312
- maternal alcohol consumption and smoking, effects, 0237
- maternal marijuana and tobacco smoking, alcohol consumption, effects, 1038
- maternal nutrition, psychosocial stress, and smoking, effect on birth weight, 0555
- maternal smoking, alcohol use, and lead exposure, effects, 1344
- maternal smoking and drinking, neurophysiological effects, 0117
- maternal stress effects in women under age 18, smoking factor, 0652
- mitochondrial proliferation in umbilical arteries, maternal smoking effect, 0171
- neuroendocrine cell innervation in lungs of smoke-exposed hamsters, 1555
- small-for-date, maternal risk factors with smoking, 0610
- thyroid function, effect of maternal smoking during pregnancy, 0423
- umbilical vein leukocytes, maternal smoking effect, 0159

NEOPLASMS
(*See also* CARCINOGENESIS; LEUKEMIA; PRECANCEROUS CONDITIONS)
- air pollution and smoking as risk factors in Shanghai, China, 0143
- alcohol consumption in Hawaiian adults, risk factor with smoking, 0830
- asbestos-exposed shipyard workers, incidence and smoking relationship, 0831
- asbestos exposure, smoking, and other risk factors in mesothelioma etiology, 0318
- benzo(*a*)pyrene-exposed pregnant mice and progeny, effects, 0820
- bone, liver, lung, and other cancers in plutonium workers, risk factors, 1187
- California physicians, cessation of smoking relationship, 0685
- cancer education programs, Quest and Assegai, for 16-year-olds in England, evaluation, 0532
- central nervous system tumors, environmental and occupational exposures as factors, 1478
- cerebral, factors in etiology, smoking relationship, 0093
- childhood exposure to cigarette smoke, risk relationship, 1313
- children with soft-tissue sarcoma, passive smoking as risk factor, 0317
- Connecticut Tumor Registry, inclusion of smoking information on all hospital patients, 0770
- cotinine and nicotine-N'-oxides, effect on tumor development in rats, 1210
- country-wide incidence and personal and regional characteristics, Switzerland, 0492
- diet, alcohol consumption, smoking as factors, prospective study in New York State, 1273
- diet, alcohol, tobacco as factors in long-term risk in middle-aged men, 1480
- environmental factors in etiology, American Cancer Society, 1195
- epidemiology data system, collection process, 1269
- epidemiology in Mormons, 0684
- ethnic groups in Hawaii, incidence and mortality, diet and smoking relationship, 0833
- etiology in industrial workers, smoking relationship, India, 0270
- gliomas in infants, passive smoking as factor in etiology, 1256
- heat-stable alkaline phosphatase as tumor marker in nonsmokers, 0636
- heat-stable alkaline phosphatase in serum and tumor tissue, 0637
- hospitalized patients, smoking, occupation, and residence relationship, 0519
- intervention and prevention program for high-risk community, 1387
- Know Your Body, program for reduction in children, effect on smoking, 1214
- lung, oral, and esophageal, incidence in high-risk areas, 0989
- malignant melanoma, heavy cigarette smoking as adverse factor in prognosis, 1073
- mastectomy patients, secondary tumors and mortality, factors, 1067
- mortality, air pollution, smoking, ionizing radiation as factors, 1410
- mortality in Israeli heart disease study cohort, 15-year followup, 0308
- mortality in Mormons, relationship to church participation, 1019
- mortality in Poland, demographic and epidemiologic factors, 0433
- mortality in women in Norway, prospective study, 0417
- mortality, risk factors determination, 0231
- mortality, smoking as factor, 0242
- multiple myeloma epidemiology, risk factors determination, 1310
- National Cancer Institute telephone communication network for smokers who want to quit, 1307
- Nebraska Laboratory Cancer Research Center, research objectives, 1154
- nitrosamines in etiology, 1206
- non-Hodgkin's lymphoma, risk relationship with smoking, 1254
- nutrition and cancer, U.S.-Finnish studies of relationship, 0986

SUBJECT INDEX

parotid gland, x-ray exposure, radiation, smoking and other factors in etiology, 0721
patients in Milan area, smoking as risk factor, 0332
personal vulnerability, perception in smokers vs. ex-smokers, 1109
personality, smoking, and other variables in patients, 0566
persons living with smokers, risk relationship, 1314
petroleum workers in Australia, occupational exposure and smoking as factors, 0035
prospective study of risk for breast, endometrial, ovarian, lung cancers in women, 1078
rhabdomyosarcoma in children, parental smoking and other environmental factors, 1306
risk associated with less hazardous cigarettes, 1299
secondary cancers, alcohol consumption and smoking as factors, 1181
selenium levels in tissues as cancer test, 0751
snuff, chewing tobacco, and cigarettes, relationship with specific cancers, 0988
snuff users, uranium content of snuff as factor, 0273
tobacco mosaic virus, role in etiology, 0151
tobacco smoking as risk factor, 0534
wives of smokers, passive smoking as risk factor, 1403

Nephritis *See* **KIDNEY DISEASES**

Nervous system *See* **CENTRAL NERVOUS SYSTEM**

NEURONS
sensory input regulation, nicotine effects, 0031
tritiated binding sites, nicotine stimulation by systemic or direct application, 0983

Neuroses *See* **NEUROTICISM**

NEUROTICISM
(*See also* PSYCHIATRIC DISORDERS)
coronary heart disease patients, effect on smoking cessation success, 0299

NICKEL
(*See also* METALS, METAL ISOTOPES)
soil and leaf levels on Ontario farms, 0062
tobacco grown on sludge-amended soil, levels, 1030

NICOTINE
(*See also* ALKALOIDS, TOBACCCO)
acetylcholine receptors in median eminence, presence and function, 1479
acetylcholine receptors, influence on neuronal expression, 0616
acetylcholine release in human placenta, effect, 1456
addictive smoking identification and nicotine gum in cessation, 0683
agricultural systems for increasing burley leaf content, 0926
airway receptors, response vs. cigarette smoke, 0893
alcohol withdrawal effects on intake, 1302
alkaloid levels, determination, 0943
allergenic extracts of tobacco leaf, content determination, 0217
amino acids in umbilical arteries and veins, inhibitory effect in smokers, 1455
antidotic substances in pine oleoresin to smoking-related injuries, 0369
arachidonic acid metabolism of human platelets and vascular endothelium, effects, 0612
arterial blood pressure regulation in rats, effect of smoke concentration, 0904
atherogenic effect in hamsters, 1203
behavioral and biochemical consequences of chronic exposure in rats, 1560
behavioral effects in monkeys, 0356
behavioral, subjective, and physiologic effects of various types of administration, 1012
binding in brain of two rat strains, comparison with acetylcholine, 1250
binding sites in brain, effect of endogenous brain material, 1252
blastocyst development alterations and uterine function effects in rats, 1111
blood platelets and leukocytes, molecular level effects, 1285
blood platelets, effect on function and catecholamine release, 0738
brain receptors, smoking effects, 0584
cardiomyopathy effects in rabbits, 0155
cardiovascular and pulmonary function, biochemical and physiological effects of nicotine-related substances, 0370
cardiovascular effects in monkeys and cats, 0264
central nicotinic receptors, location and function, 0983
chemosensitivity of crayfish stretch receptors, 0892
chewing gum, efficacy in treatment of ulcerative colitis in ex-smokers and nonsmokers, 1239
chewing gum, smoking cessation efficacy, 0027
cocarcinogenic effects in mice, 1238
coronary blood flow relative to myocardial oxygen demand, effect, 1408
coronary disease risk in pipe and cigarette smokers, 0534
dependent smokers, efficacy of 2 mg vs. 4 mg nicotine gum for cessation, 1355
dialyzability in human subjects, 1437
distribution and kinetics in pregnant sheep and fetus, 0672
duodenal mucosal blood flow, cigarette smoke and i.v. adminstration effects in rats, 0748
electroencephalogram response, 0744
emphysema, toxicological investigation of causal relationship, 0900
endocrinological and biochemical responses to intravenous administration in rabbits, 1021
endothelium-platelet-tumor cell interactions, 0613
epithelial cell damage, effect of single injection vs. continuous infusion, 0537
flavor aversion in rats and hamsters, route of administration effect, 1188
gastrointestinal processes, effects with cadmium, 0628
genetics of tolerance, function of brain nicotinic receptors, 0757
heart function effects, 0210
hemodynamic actions on canine stomach, 1358
hippocampal 5-HT systems, role in behavioral responses to nicotine in stressed rats, 0587
histamine and serotonin levels in serum of dogs, effect, 0377
hormones, effect with benzo(*a*)pyrene on normal and ectopic production, 1064

- hyperglycemina induction in diabetic vs. healthy smokers, 0141
- hypnosis in reduction of intake, effectiveness, 1325
- individual differences in sensitivity, 0897
- indoor air concentrations as passive smoking index, variability, 0376
- information processing in humans, nicotine tablet effect, 0574
- intestinal blood flow and oxygen consumption in dogs, effect, 1357
- main and digital blood vessels, effects, 0842
- NAD(P) glycohydrolase role in exchange reaction with nicotinamide, 1050
- nasal solution as aid in smoking cessation, 0522
- neuroendocrine effects in humans, 0746
- opioid peptides, regulation of oxytocin and vasopressin, effect, 1392
- Parkinson's disease, possible beneficial effect, 1251
- peripheral chemoreceptors, stimulation, 0365
- pharmacologic treatment agents for nicotine dependence, 0638
- plasma levels and symptoms of intolerance, 0632
- plasma levels, cigarette yield and other determinants, 0905
- plasma levels, compensation in smokers who switch to low-yield brands, 1215
- plasma levels following exposure to cigarette smoke or nicotine gum, 0629
- plasma levels in brand switchers, changes over study period, 1017
- plasma levels in pregnant ewes, chronic smoke exposure effects, 0671
- plasma lipoprotein composition and metabolism in monkeys, oral administration effects, 1082
- platelet function effects, 0230
- preference following deprivation and satiation, 0737
- primate physiology and behavior, effects, 0817
- prostacyclin production in kidney, lung, and vascular bed, inhibitory effects, 0500
- psychopharmacology of nicotine sulfate in rats, 1562
- psychophysiological and psychological correlates of nicotine-seeking behavior, 0694
- radioimmunoassay for determination, 1049
- receptors in rat brain, isolation and characterization, 1286
- reinforcing properties, behavioral effects in rats, 0909
- renal failure effect on blood levels following smoking, 1438
- respiratory effects in cats and monkeys, 0265
- schedule-controlled responding in dogs and squirrel monkeys, effect, 1014
- seborrhoeic dermatitis, allergic reaction as etiologic factor, 0247
- self-administration in dogs, behavioral effects, 1013
- self-administration in rats as model of tobacco dependence, 0249
- sidestream smoke exposure, dose-related absorption and excretion, 1209
- smooth muscle cells, physiological effects, 1093
- sperm motility in smokers, effect, 1454
- stereoisomers, chromatographic separation and comparative metabolism, 0760
- stereoselective studies of (+)- and (-)-nicotine in rats, 1511
- stress reduction effectiveness in light vs. deep inhalers, 0483
- sweet food intake in rats following cessation of nicotine administration, 1020
- thromboxane and prostaglandin synthesis effects, 0452
- titration in tobacco dependence, smoking characteristics in adolescents vs. adults, 0705
- transdermal doses, effect on cigarette craving and nicotine preference, 0756
- urine and plasma concentration as smoking status determinant, 0215
- urine and plasma levels in smokers vs. nonsmokers, 0375
- urine levels, effect of renal function impairment, 1433
- ventilatory response to hypercapnia in dogs after intravenous injection, 0389
- vertebral blood flow in dogs, effect of nicotine lactate, 1500
- visual and auditory sensory input regulation, effects, 0031
- withdrawal from chronic doses in rats, detection of subjective symptoms, 1468

Nicotine chewing gum *See* **TOBACCO SUBSTITUTES**

NICOTINE CONTENT
- acute respiratory effects of cigarette smoke inhalation in awake dogs, relationship, 0917
- arterial and capillary blood flow in skin, effect, 0914
- blood levels in smokers of low-yield vs. high-yield cigarettes, 0522
- British cigarettes, changing levels, 0527
- chemical analysis of tobacco leaf, 0950
- chutta tobacco from southeast India, 0278
- cigarette preference relationship, with sweet-bitter taste dimension, 0795
- cigarettes from developing countries, WHO-sponsored analysis, 0496
- domestic and imported cigarettes in Australia, 0007
- Egyptian cigarettes, reduction following legislation, 0173
- inhalation and puffing patterns, effect of varying levels, 0992
- Italian cigarettes, 0331
- lanka tobacco leaf and smoke, India, 0268
- leaf aging time effect, 0267
- myocardial infarct survival relationship, international study, 0547
- near infrared spectrosocpy of tobacco and tobacco products, 1318
- platelet function effects, cigarette level as factor, 0230
- prostacyclin and thromboxane balance in cardiovascular system, smoke level effect, 0668
- reduced levels, effect on bronchial epithelium of smokers, 1177
- short-term thermal treatment system for tobacco expansion, reduction effect, 0442

NICOTINE DERIVATIVES
(*See also* COTININE; NORNICOTINE)
- carcinogenesis of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone in rats, 1206
- chemistry, reactions and metabolites, 0477
- N-nitrosonornicotine, nitrogen fertilization effect on level, 0826
- nicotine-N′-oxides and cotinine, effect on tumor development in rats, 1210
- nitrosonornicotine, metabolism and DNA adduct formation, 1205
- nitrosonornicotine, skin and oral mucosa permeability, 0875
- snuff and chewing tobaccos in Sweden, levels in 1981-1983, 0466

NICOTINE METABOLISM
(*See also* DRUG METABOLISM)
- blood analysis after smoking in hemodialysis patients and healthy volunteers, 1437
- cholinergic and dopaminergic activity in the central nervous system, 0941

chromatographic separation and comparative metabolism of d- and l-nicotine, 0760
lung tissues of animals and humans, bioactivation, 0708
rat liver cells, transport mechanisms of uptake and metabolism, 1284
renal function, effect on nicotine urine levels, 1433
tobacco-insect interaction model, 1034
urine levels in rats in study of biochemical defense mechanisms, 0889

NICOTINE PHARMACOLOGY
behavioral profile as a prototypic dependence-producing drug, 1012
binding sites in rat brain and central nervous system, 0910
biochemical consequences of chronic exposure in rats, 1560
body weight changes following smoking cessation, relationship, 1020
brain areas of nicotine sites of action, cholinergic vs. noncholinergic, 1514
brain nicotine receptors and neurotransmitter systems, behavioral effects in rats, 0521
central nervous system effects, 1107
flavor aversion in rats and hamsters, route of administration effect, 1188
intravenous administration in rabbits, endocrinological and biochemical responses, 1021
leukotriene D_4 receptors in peripheral lung and alveolar macrophages, effects, 1153
mask and smoke dosage apparatus for effects in rabbits and small rodents, 0368
neuromuscular effects of tobacco chewing and snuff-dipping, 1463
neuropeptide secretion in mouse brain, behavioral effects, 0763
nicotinic ligand binding in brain tissue, 0520
norethisterone and ethynylestradiol as inhibitors of conversion to cotinine, 1049
steroid hormones, interactive behavioral and motor effects in mice, 0818
subcortical self-administration in rats, taste aversion and other behavioral effects, 0909
subjective effects in animals, mechanisms, 1406
tolerance and dependency mechanisms, 0941

NICOTINE REDUCTION
genetic method in tobacco growing, 1331

NICOTINISM
psychomotor task response inhibition during smoking deprivation, 1136

Nicotine withdrawal *See* **WITHDRAWAL SYMPTOMS**

NITRATES
(*See also* NITROSAMINES)
aromatic amines formation in cigarette smoke, influence, 1202
chemical analysis of tobacco leaf, 0950
determination in biological media, 1404
determination method for foods and snuff, 1291
extraction from tobacco leaf, procedure, 1034
leaf-curing effects, 0881
removal from Maryland tobacco, curing procedure, 1035

NITROGEN COMPOUNDS
biochemical effects and toxicity of nitrogen oxides and nitrosyls, 1470
nitrosamine formation and inhibition, chemical processes, 1144

NITROGEN CONTENT
burley, slow-release fertilization, effects, 0944
burley tobacco, microbial nitrate reduction and nitrite production, 0951
burley tobacco, nitrogen and potassium addition effects, 0946
carbon/nitrogen ratio and tobacco leaf components, 0921
chemical analysis of tobacco leaf, 0950
chutta tobacco from southeast India, 0278
near infrared spectroscopy of tobacco and tobacco products, 1318
nitrosonornicotine formation in tobacco leaf, effect, 0945
soil water stress effect, 0953

Nitrogen dioxide *See* **NITROGEN OXIDES**

NITROGEN OXIDES
cigarette structural alterations to reduce yield, 0928
electron transfer processes, biochemical effects, 1470
nitric oxide activation of guanylate cyclase, 0740
ozone and nitrogen dioxide, long-term exposure effects on lung function in monkeys, 0653

NITROSAMINE CONTENT
N-nitrosodiethanolamine levels in tobacco products, 1197
nitrogen management effect, 0945

NITROSAMINES
(*See also* NITRATES)
analytical procedures for determination in biological media, 1404
assay method for carcinogenesis testing in animal tissues, 1199
biochemical mechanisms of carcinogenesis, 1353
biochemical pathway for chain-shortening reactions of β-oxidized nitrosamines, 1145
bladder cancer induction in rats, catechol administration effect, 1210
carcinogenesis, 1206
carcinogenesis, project overview, 1207
carcinogenesis, screening for inhibitors, 1201
chemical processes involved in formation and inhibition, 1144
determination method for foods and snuff, 1291
electron transfer processes, biochemical effects, 1470
esophageal carcinogenesis promoted by catechol in rats, 1160
ethanol consumption in rats, cocarcinogenicity, 1204
formation in saliva of areca chewers, 1196
indoor air pollution, sidestream smoke as source, 0387
inhibition of localization in tumor sites by alcohols, 0936
mainstream and sidestream smoke, quantification method, 1211
metabolism and hormonal regulation in liver and kidney, 0782
metabolism of intermediates, DNA damage, and carcinogenic process, 1205
mutagenic activity in rat lung, effect with alcohol consumption, 1293
N-nitrosoproline, nitrosation potential of inhaled cigarette smoke, 1208
NDMA, N-PYR, NNN administered to nursing rats, transfer to suckling DNA and RNA, 0001

- pharmacokinetics of tobacco-specific nitrosamines, 1200
- pulmonary and hepatic damage, chemoprotection by dietary indoles, 1360
- snuff constituents, carcinogenicity in rats, 0993
- volatile and particulate phases of cigarette or tobacco smoke, determination, 0822
- volatile and tobacco-specific, levels in Swedish snuff and chewing tobacco 1981-1983, 0466

NONSMOKERS
- Amish in Pennsylvania, lung cancer mortality vs. non-Amish population, 1398
- coronary artery disease patients, acute effects of carbon monoxide exposure, 0649
- cough, eye irritation associated with workplace passive smoking, 1351
- female lung cancer patients, passive smoking, air pollution, diet as risk factors, 0256
- heat-stable alkaline phosphatase as tumor marker, 0636
- heat-stable alkaline phosphatase, serum level vs. smokers, 0637
- Hong Kong Chinese women and Japanese women, lung cancer risk factors, 0257
- housemates, effect on cessation attempt in clinic program, 1110
- longevity in men vs. women, 1397
- lung cancer, passive smoking and occupation as risk factors, 1295
- lung cancer risk in female nonsmokers in Sweden, factors, 0459
- lung function, passive smoking effects, 0018
- middle-aged cohort in Scotland, passive smoking as factor in symptoms, 0591
- national, state, and local rights groups, legislative impact, 1342
- respiratory symptoms from moderate and heavy smoke exposure, influence of suggestibility, 0126
- ulcerative colitis patients, efficacy of nicotine chewing gum in treatment, 1239
- urinary cotinine levels, passive smoking factor, 0245
- wives of smokers, cancer risk relationship, 1403
- wives of smokers, lung cancer risk, 0254
- women married to smokers, coronary disease risk relationship, 0698
- women married to smokers vs. ex-smokers vs. nonsmokers, long-term followup, 0701

Noradrenaline *See* CATECHOLAMINES

Norepinephrine *See* CATECHOLAMINES

NORNICOTINE
- (*See also* NICOTINE DERIVATIVES)
- alkaloid levels, determination, 0943
- carcinogenesis, screening for inhibitors, 1201
- diastereomeric derivatives separation for comparative metabolism of d- and l-nicotine, 0760
- lanka tobacco of India, levels, 0268
- nitrogen fertilization effect on N-nitrosonornicotine level, 0826
- nitrosonornicotine localization in epithelial tissues in mice, 0935
- schedule-controlled responding in dogs and squirrel monkeys, effect, 1014
- skin and oral mucosa permeability to nitrosonornicotine, 0875
- snuff and chewing tobaccos in Sweden, levels in 1981-1983, 0466
- unburned tobacco levels, determination method, 0822

NOSE NEOPLASMS
- (*See also* RESPIRATORY TRACT NEOPLASMS)
- alcohol consumption and N'-nitrosonornicotine treatment in rats, 1204
- occupational exposure and smoking as risk factors, 0457
- occupational exposure to formaldehyde as factor, smoking relationship, 1518
- occupational exposures, risk with smoking and alcohol consumption, 0720

NUCLEIC ACIDS
- (*See also* DNA)
- benzo(*a*)pyrene binding, structure of adducts formed, 1159
- conformational features following modification by carcinogens, 1174
- deoxyguanosine-BaP and deoxyadenosine-BaP adducts, removal from DNA, 1155
- 7H-dibenzo(*c*, *g*)carbazole binding, 1359

Oat cell carcinoma *See* CARCINOMA, BRONCHOGENIC

OBESITY
- (*See also* BODY WEIGHT)
- cardiovascular disease risk factor with smoking, family diagnosis and therapy, 1356
- coronary artery disease risk factor in sedentary males who smoke, 1442
- elderly women, hematological effects, with smoking, 0885
- following tobacco withdrawal, causes, 0463
- heart disease risk factor, with smoking, Australian survey 1980, 0016
- kidney cancer risk factor, 1060
- North Dakota telephone risk factor prevalence survey, 1338
- prevalence in inpatients, relationship with smoking habit, 1441

OBSTRUCTIVE AIRWAY DISEASES
- (*See also* BRONCHIAL DISEASES; EMPHYSEMA)
- age, duration of asthma, atopy, and smoking in etiology, 0511
- air pollution, aeroallergens, smoking, and meteorologic conditions as factors, 0618
- alcohol consumption and smoking effect on mediators of inflammatory response, 0913
- alpha$_1$-antitrypsin levels in patients, 1148
- alveolar hypoxia relationship, 1138
- bronchitis, smoking relationship, 0182
- cessation of smoking effect on natural disease history, 0622
- chronic bronchitis vs. airways obstruction, differences in risk factors, 1005
- diurnal rhythms in obstruction, sputum production, atopic status, and smoking effects, 0512
- environment, heredity, smoking, occupation, and childhood diseases as risk factors, 0617
- genetic and epidemiologic differences in smokers vs. nonsmokers, risk relationship, 0998
- histamine responsiveness as early indicator of airflow obstruction, 0043
- irreversible air flow obstruction, elastolytic activity in smokers vs. ex-smokers, 0302

lung cancer risk relationship, smoking as factor, 1006
lung function changes in nonsmokers, ex-smokers, and smokers, 1419
lung structure and function in smokers vs. nonsmokers, pathophysiological mechanisms, 0619
metoprolol and propranolol effects on lung function in patients, 0621
subjective and objective measurement of smoke inhalation, disease relationship, 0791
transit time analysis of forced expiration after H_2O mist exposure for diagnosis, 0329

OCCUPATIONAL DISEASES
(*See also* BRONCHIAL DISEASES; EMPHYSEMA)
acute and chronic diseases in tobacco factory workers, dust exposure relationship, 0167
asbestos-related biomarkers to determine risk index, 0678
asbestosis in saltpeter workers, effect of exposure and smoking, 0413
asthma in snow crab processing workers, smoking as added risk factor, 0084
bladder cancer in industrial workers, occupational exposure as risk factor with smoking, 0164
bladder cancer, risk factors determination, 0091
bronchial atypia in soot and BCME exposed workers, smoking as factor, 0444
cancer, exposure as risk factor with smoking, 0960
cancer in asbestos-exposed shipyard workers, smoking relationship, 0831
cancer in Canadian miners, exposures and smoking as factors, 0097
cancer in petroleum workers in Australia, smoking habit relationship, 0035
cancer in steel plant workers, exposures and smoking as factors, 1425
cancer in uranium miners, radon exposure and smoking as risk factors, 0242
cancer incidence in industrial workers (India), smoking related, 0270
cancer prevention in asbestos-exposed workers with lung disease, 1531
carbon monoxide poisoning, occupational exposures and smoking as factors, 0440
carcinogen levels in industrial workers, smoking effect, 0402
central nervous system tumors, occupational exposure as factor, 1478
cerebral tumors in farming, rubber, and plastics industries,, smoking as factor, 0093
coal workers' pneumononiosis, 1546
farmers' lung disease, antibody titers in smokers vs. nonsmokers, 0366
head and neck cancer, alcohol consumption, smoking, and occupation as factors, 0070
high blood pressure in noise-exposed workers, smoking and other factors, 1418
immune system changes in noise-exposed workers, smokers vs. nonsmokers, 0438
ischemic heart disease in aluminum workers, chemical exposure and smoking as factors, 0087
lung and laryngeal cancer in Polish workers, alcohol consumption and smoking as factors, 0432
lung cancer, exposure as risk factor with smoking, 0034 1388
lung cancer in miners, blood test as screening tool for early detection, 0116
lung cancer in persons passively exposed to smoke, risk, 0783
lung cancer in plutonium workers, smoking effect, 1187
lung cancer in steel workers, detection/prevention, 0635
lung cancer in uranium miners, 0656
lung cancer in uranium miners, radiation and smoking as risk factors, 1189
lung cancer in women, smoking relationship, 0092
lung diseases and immunologic abnormalities in asbestos-exposed workers, smoking as factor, 0429
lung diseases in coal miners, prevalence and longitudinal change, 15-year followup, 1545
lung function decline in firemen, smoking as factor, 0509
lung function decline in iron workers, smokers vs. nonsmokers, 0221
melanosis in lead workers, smoking as factor, 0381
mesothelioma in asbestos-exposed workers, smoking relationship, 0318
mortality in cadmium-exposed workers, 0529
nasal and laryngeal cancer, exposures and smoking as factors, 0457
nasopharyngeal neoplasms, exposure factors with smoking and alcohol consumption, 0720
pancreatic cancer, chemical exposure, 0467
peptic ulcers in Japanese factory workers, smoking as factor, 0382
pleural plaques in asbestos-exposed workers, smoking relationship, 1389
pneumoconiosis in coal workers, role of lung proteases and antiproteases, 1247
polymer fume disease in exposed workers, smoking habit relationship, 1429
respiratory abnormalities in asbestos workers, smoking as factor, 0096
respiratory cancer, blue-collar industrial risks, 0665
respiratory cancer in formaldehyde-exposed workers, smoking as factor, 1518
respiratory disease in cab drivers, risk factor identification, 0241
respiratory disorders in poultry workers, dust exposure and smoking association, 0465
respiratory impairment in coal miners exposed to diesel fumes, smoking effect, 1544
respiratory, smoking relationship, 0017
urogenital cancer, industrial exposure risk with smoking, 0344

OCCUPATIONS
aluminum workers, 0087
asbestos-exposed workers, 0470
asbestos workers, 0096
asbestos workers, 1223
bakers, 0248
BCME-exposed workers, 0444
cab drivers, 0241
cadmium-exposed workers, 0529
chloromethyl ether-exposed workers, 1388
coal miners, 1544
copper smelter workers, 1244
doctors, 0173
emergency medical technicians, 1362

  factory workers in Japan, 0382
  farmers, 0366
  firemen, 0509
  fluorescent plant workers, 0086
  forestry workers exposed to phenoxy acid herbicides, 0196
  health service personnel, 0518
  industrial workers, 0270
  iron miners, 0221
  lead workers, 0381
  male theologians in Norway, 0407
  medical services workers in China, 0149
  miners, 0470
  nurse practitioners, 0771
  nurses, 0025 1124
  pentachlorophenol-exposed workers, 0177
  petroleum workers, 0035
  plutonium workers, 1187
  polytetrafluoroethylene workers, 1429
  postal workers, 1223
  railroad workers, 0677
  saltpeter workers, 0413
  shipyard workers, 0678
  snow crab processing workers, 0084
  soldiers, 0539
  soot-exposed workers, 0444
  steel workers, 0635
  sulfur dioxide-exposed workers, 1061
  teachers, 0173
  thermoelectrical plant workers, 0333
  tobacco factory workers, 0167
  uranium miners, 0097
  workers exposed to electric and magnetic fields, 0177

Opsonins *See* ANTIBODIES

Oral contraceptives *See* CONTRACEPTIVES, ORAL

ORAL HYGIENE
  (*See also* PERIODONTAL DISEASES)
  cancer risk factor, with diet, alcohol consumption, and smoking, 1274
  periodontal diseases, risk factor with smokeless tobacco use, 0819

Oral neoplasms *See* MOUTH NEOPLASMS

Orbital neoplasms *See* EYE NEOPLASMS

Osteoporosis *See* BONE DISEASES

OVARIES
  (*See also* UROGENITAL SYSTEM)
  enzymatic metabolism of benzo(*a*)pyrene, 0626

OXYGEN TRANSPORT
  arterial oxygen saturation in healthy smokers vs. nonsmokers, 0602
  arterial wall, carbon monoxide effect on arteriosclerosis etiology, 0839
  baboon mothers who smoke, fetal effects, 1231
  diabetic women during pregnancy, smokers vs. nonsmokers, 0156
  exercise capacity, smoking effect, 0640
  nicotine effect on blood flow and embryo development in rats, 1111

PANCREAS
  carcinogen metabolism in human, rat, and hamster cell culture, 1163
  enzyme activity after benzo(*a*)pyrene treatment, 0827
  responsiveness and susceptibility to secretin in heavy smokers, 0734

Oropharyngeal neoplasms *See* PHARYNGEAL NEOPLASMS

Palmitic acid *See* FATTY ACIDS

PANCREATIC NEOPLASMS
  adult smoking prevalence, temporal relationships, 1390
  alcohol consumption, chemical exposures, and smoking relationships, 0467
  diet, tobacco use, alcohol consumption, and other risk factors, 0036
  enzyme activity in 7, 12-dimethylbenz(*a*)anthracene-induced adenocarcinomas in rats, 0871
  etiology, tobacco and other environmental factors, 0858
  Nebraska Laboratory Cancer Research Center, objectives, 1154
  nutrition, occupation, residence, and smoking as risk factors, 0960

Paraganglioma *See* NEOPLASMS

Paralysis agitans *See* PARKINSONISM

PARENTAL SMOKING
  (*See also* MATERNAL SMOKING; PATERNAL SMOKING; SMOKING)
  acute otitis media with effusion in infants, relationship, 1324
  adolescent smoking initiation, effect of habit and attitudes, 0236
  adolescents in Athens, effect on smoking habits, 0251
  asthma and airway function in second and fifth graders, effect with air pollution, 0723
  carbon monoxide levels in expired air of children, indicator of passive smoke exposure, 0569
  child development at age 10, relationship, 1192
  childhood rhabdomyosarcoma, risk factor with other environmental agents, 1306
  children grades K-6, effect on attitudes and behavior, 0779
  health education program to reduce infant exposure, efficacy, 0029
  leukemia and soft-tissue sarcoma in children, risk relationship, 0317
  Minnesota Heart Health Program, effect of intervention strategies, 1135
  passive smoking risk in infants, efficacy of health education for reduction, 0030
  postprandial colic in infants, relationship, 0225
  postprimary schoolchildren in Dublin, factor in smoking initiation and maintenance, 0294
  prevention/intervention services for children of substance-abusing families, 1493
  respiratory infections in children, risk relationship, 1287
  respiratory symptoms and lung function in children, relationship, 1105
  respiratory system effects in children, with gas cooking, 0870

SUBJECT INDEX

PARKINSONISM
nicotine and cigarette smoke components, possible beneficial effect, 1251

Particulate matter *See* **TARS, CIGARETTE; TARS, TOBACCO**

PASSIVE SMOKING
adenocarcinoma risk relationship in adult women in Shanghai, 0142
airway reactivity and frequency-dependent compliance in smoke-exposed lambs, 0793
asthma and airway function in second and fifth graders, relationship, 0723
asthmatic children, effects, 0076
bibliography of research on nature and health effects, 0710
brain tumors in children and adolescents, risk relationship, 0733
cancer risk in adults following childhood exposure, 1313
cancer risk in persons living with smokers, 1314
cardiovascular, respiratory, psychomotor responses in humans and rabbits, 0371
children aged 10 and 11, measurement by expired carbon monoxide, 0569
children aged 8 to 16, long-term effects, with/without air pollution, 0435
children and household members, lung function effects, 0689
children, lung function effects, 0049
children with leukemia or soft-tissue sarcoma, risk relationship, 0317
Chinese female lung cancer patients, risk relationship, 0259
chronic obstructive lung disease, risk relationship in Greek women, 0255
cotinine in blood as marker of exposure, 0522
employees, attitudes and complaints, 1351
environmental tobacco smoke, risks, 1207
families of asbestos workers in Los Angeles, lung function effects, 0722
gliomas in infants, risk relationship, 1256
home, workplace, public areas, measurement, 0380
indoor air pollutant, effective reduction through reduced smoking, 0775
infants, acute otitis media with effusion, relationship, 1324
infants, health education of parents for reduction, efficacy, 0029
infants, parental smoking as respiratory illness and viral infection risk factor, 1462
infants, postprandial colic relationship, 0225
infants with bronchiolitis, asthma risk relationship, 0023
information kit to promote smoke-free areas in workplaces, 0063
interferon production effects in tissue cultures and mice, 0939
lung cancer risk factor, 0092 0783
lung function effects, 0018
nicotine concentrations in indoor air as exposure index, variability, 0376
nonsmokers' rights groups, survey of legislative impact, 1342
pamphlet of health effects for health providers, 1539
pregnant women, thiocyanate as indicator of exposure, 1471
Project VOTE, Kansas program to reduce occupational exposure, 0876
pulmonary function responses in nonsmokers, influence of suggestibility, 0126
respiratory and cardiovascular symptoms in middle-aged cohort in Scotland, effect, 0591
selected methods of analysis, International Agency for Research on Cancer report, 0250
tobacco mosaic virus in inhaled smoke, role in disease etiology, 0151
urinary cotinine levels in nonsmokers, relationship, 0245
urine mutagenicity, chromosomal damage, and other biological effects, 0194
wives of men who smoke, chronic respiratory disease relationship, 0280
wives of smokers, cancer risk relationship, 1403
women married to smokers, coronary disease risk relationship, 0698
women married to smokers, long-term followup of mortality and morbidity, 0701

PATENTS
carbon monoxidase for detection and conversion of carbon monoxide in tobacco smoke, 1303
filter with acceptable pressure drop for low tar cigarettes, 0383

PATERNAL SMOKING
(*See also* PARENTAL SMOKING; SMOKING)
cancer risk relationship in adult offspring, 1313

PEER GROUPS
adolescent health education, effect on smoking initiation, 1062
adolescent drug use, influence, 1232
adolescent, perceived pressure effect on smoking initiation, 1112
adolescent substance use/abuse, factor with family and sibling attitudes and behaviors, 1134
adolescents, effect on smoking habit, 0131
children aged 10 to 12 in Australia, influence on smoking habits, 0040
females, effect with paternal and family factors in drug and tobacco use, 1222
fourth graders, high school students as leaders of antismoking program, 1217
junior/senior high school students, influence on smoking behavior, 0873
medical students as antismoking counselors for high school students in Israel, 0304
Napa Drug Abuse Prevention Project, evaluation of influence, 0647
postprimary schoolchildren in Dublin, factor in smoking initiation and maintenance, 0294
seventh grade students in Canada, leadership of smoking prevention program, 0083
sixth graders, peer leaders as prevention of smoking instructors, 1364

PEPTIC ULCER
(*See also* GASTROINTESTINAL DISEASES)
attributable risk in cigarette smokers, males vs. females, 0650
Japanese factory workers, smoking as factor, 0382

PERCEPTION
(*See also* COGNITION)
adolescents in Israel about smoking, intervention program effect, 0310
adolescents, smoking initiation relationship, 0696

adolescents' views of smokers, advertising influence, 0669
cigarette advertising, effect of viewing "Death in the West" in children, 0709
employee complaints in smoking-permitted vs. smoking-restricted offices, 0099
general practitioners, nurses, educators of health behavior, smoking habit relationship, 0401
health status by elderly blacks in the inner city, smoking habit relationship, 1175
housemates' support of cessation attempt, perception as factor, 1110
irritability of passive smoke exposure in nonsmokers, influence on respiratory symptoms, 0126
low-tar cigarettes and advertising, effect on adolescent smoking habits, 0505
neighborhood setting perception as factor in drug use by inner-city students, 0798
personal vulnerability to health hazards of smoking, effect on cessation, 1109
self-efficacy in adolescents, predictor of smoking behavior, 0851

Perinatal mortality *See* INFANT MORTALTIY

PERIODONTAL DISEASES
(*See also* DENTAL DISEASES; ORAL HYGIENE)
adolescents in Sweden, smoking and snuff use relationship, 0456
chewing tobacco use relationship, 1405
cigarette, pipe, and cigar smokers, differential effects, 1097
gingivitis, inflammatory vascular reaction in smokers vs. nonsmokers, 0455
nicotine chewing gum for smoking cessation, risk relationship, 1348
oral microorganisms in etiology, effect of smokeless tobacco extracts, 1029
smokeless tobacco use, risk relationship, 0819
smokers' melanosis, gingival epithelium ultrastructure, 0461

PERSONALITY
(*See also* BEHAVIOR, HUMAN)
addicted smokers, identification and cessation predictors, 0683
adolescent, predictability of smoking patterns as adult, 0674
adolescents, changes over time as factor in drug use, 1248
adolescents, effect with advertising on smoking attitudes, 0669
adolescents, survey of influence on smoking initiation, 0716
cancer patients, factor with smoking and other variables, 0566
cessation of smoking methods most effective for different types of smokers, 1170
cessation of smoking self-quitters, 0325
characteristics of smokers vs. nonsmokers vs. ex-smokers, 0350
childhood temperament as predictor of marijuana, alcohol, and tobacco use, 1394
coronary disease risk relationship, 5-year followup study, 1277
extroverts vs. introverts, interactive effects of smoking, 0567
health locus of control and cessation of smoking after bypass surgery, 1332
health locus of control and followup letters to maintain smoking abstinence, 1337
health locus of control and self-esteem as factors in smoking cessation, 1335
individual differences and cessation attempts following exposure to antismoking materials, 1334
Kuopio Ischaemic Heart Disease Risk Factor Study, 0204
male vs. female long-term smokers vs. ex-smokers vs. never smokers, 0670
motor task performance by smokers, effect with stress, 0530
neuroticism and extroversion, smoking relationship 0560
nicotine sensitivity, relationship, 0897
nonsmokers vs. ex-smokers vs. social smokers vs. heavy smokers vs. recidivists, 1349
Normative Aging Study in middle-aged men, longitudinal effects, 1046
nurses in South Africa, possible factor in decision to smoke, 0447
paternal characteristics, effect on daughter's drug and tobacco use, 1222
physicians, correlates of smoking initiation and cessation, 1308
postprimary schoolchildren in Dublin, factor in smoking initiation and maintenance, 0294
psychological characteristics of heavy smokers, 0501
puffing behavior of inhalers vs. noninhalers, relationship, 0485
sedative vs. stimulant smokers, factor in smoking behavior, 0561
self-efficacy score as predictor of success in cessation of smoking, 0046
sensation seekers vs. sensation avoiders, cessation of smoking program elements, 0786
sensory input regulation, smoking relationship with extraversion, 0031
seventh graders, smoking prevention curriculum, factor in efficacy, 1234
sex-related differences in ex-smokers, 0655
smoking cessation effects in group sessions, 0741
spectral analysis for assessment of smoker subtypes, 0852

PESTICIDES
(*See also* AGRICULTURAL PRACTICES; TOBACCO CONTAMINANTS)
chemical composition effects on tobacco leaf, 0948
cured tobacco and tobacco smoke, residues, 1317
engineering aspects of control, 1328
reduction of hazards through biological research, 1304
reduction with chemical means, 1451
residue reduction, breeding methods, 1556
soil and leaf levels on Ontario farms, 0062
soil-borne diseases of tobacco, control methods, 0824

PHAGOCYTOSIS
(*See also* MACROPHAGES; PULMONARY ALVEOLAR MACROPHAGES)
synergistic effect of cigarette smoke and silica dust exposure, 0475

PHARMACOKINETICS
dopamine and tyrosine hydroxylase activity in rat brain, nicotine effect, 0941
histamine H_2-blockers, smoking effect, 0580
tobacco-specific nitrosamines, 1200

SUBJECT INDEX

PHARYNGEAL NEOPLASMS
(*See also* NASOPHARYNGEAL NEOPLASMS; RESPIRATORY TRACT NEOPLASMS
- added risks in patients who continue to smoke, 0702
- alcohol consumption and smoking as risk factors, early detection techniques, 1181
- alcohol consumption in nonsmokers, risk relationship, 1183
- levels of IgA and its secretory component in patients, 1333
- males in India, bidi smoking relationship, 0271
- occupational/residential exposure as factor, smoking association, 1518
- reverse (chutta) smoking as risk factor, 0276
- screening project for smokers over age 40, 0938
- second primary cancer in patients, smoking as risk factor, 0715
- tobacco chewing in Pakistan, risk relationship, 0424
- women in India, snuff use relationship, 0269

PHARYNX
- normal bacteria, in vitro effects of cigarette smoke exposure, 1168

PHENOL CONTENT
- commercial cigarettes, rapid, accurate determination procedure, 1447
- sidestream and mainstream smoke, distribution ratio, 0374

PHENOLS
(*See also* ALCOHOLS)
- blue mold effects on tobacco constituents, 0930
- catechol and polyphenols in tobacco, genetics and breeding, 1321
- catechol effect on nitrosamine-induced carcinogenesis in rats, 1160
- volatile and particulate phases of cigarette or tobacco smoke, determination, 0822

Phospholipids *See* **LIPIDS**

PHYSICAL ACTIVITY
- adult Americans, measure of health strategies and behaviors, 1396
- aerobic exercise as intervention strategy for smoking cessation, 0135
- athletes in various sports, smoking prevalence, 0316
- carbon monoxide and smoke inhalation, acute effects during maximal exercise, 0169
- cardiovascular function, ventilation, gas exchange during exercise, smoking effect, 0640
- cardiovascular response to beta adrenoreceptor blockade in smokers and nonsmokers, 0601
- coronary disease risk in overweight, sedentary males who smoke, 1442
- coronary heart disease risk relationship, 0058
- diabetic adolescents, cardiovascular disease risk evaluation, 1417
- endurance tests, smoking effect under normal and low atmospheric pressure, 0206
- health care personnel training in Finnish village, effect, 0205
- Healthstyles program to promote health-enhancing behavior, 0074
- high density lipoprotein cholesterol, effect with cigarette smoking, 0942
- Kuopio Ischaemic Heart Disease Risk Factor Study, 0204
- middle-aged men in Sweden, heart disease and cancer risk relationship, with smoking, 0474
- noise reactivity effect vs. mental stress vs. smoking, 0486
- participation 12 months post-cessation of smoking, abstinence relationship, 1452
- peripheral vascular disease patients, intervention program effectiveness, 1294
- pregnant women, effect on outcome, 0077
- premenopausal women, effect with alcohol use and smoking on lipoprotein cholesterol, 0934
- protection against myocardial infarct, smoking relationship, 0718
- reliability of long-term recall in prevention programs, 0661
- respiratory function relationship in smokers vs. nonsmokers, 0252
- smoking habit relationship, 0813
- worksite cessation program, factor in abstinence, 0691

PHYSICAL FITNESS
- army medical company personnel, smoking habit relationship, 1290
- Army Physical Readiness Test, smokers vs. nonsmokers, 1466
- cardiovascular disease risk factor relationship, with smoking, 0078
- coronary heart disease risk relationship, 0058
- exercise program and smoking cessation, long-term effect, 1452
- group counseling smoking cessation program participants, outcome effects, 0135
- training of athletes, factor in smoking initiation, 0316

PIPE SMOKING
(*See also* SMOKING; TOBACCO SMOKE)
- bladder cancer risk relationship, 1009
- lung cancer risk relationship vs. cigarette vs. cigar smoking, 0228
- males in Switzerland, changes between age 19 and age 31, 0494
- myocardial infarct and angina patients, effect on long-term morbidity, mortality, 0301
- pancreatic, bile-duct, and gallbladder cancer risk relationship, 0246
- periodontal health, effects vs. cigarette smoking, 1097

PLACENTA
- acetylcholine release, nicotine effect, 1456
- amino acid profiles in smokers vs. nonsmokers, 1455
- benzo(*a*)pyrene-DNA adducts, smokers vs. nonsmokers, 0216
- cadmium exposure in smokers, effect on zinc level, 1345
- detoxification systems, activities and molecular characteristics, response to smoke, 0758
- leukocytes in blood from smokers vs. nonsmokers, 0159
- newborns of mothers who smoked during pregnancy, blood vessel changes, 0184
- nicotine and cotinine transfer and metabolism in pregnant sheep and fetus, 0672
- oxidase activities, maternal smoking as stimulus, 1346
- pharmacokinetics and toxicity of environmental agents, 1288
- pinocystolic activity in smokers vs. nonsmokers, 0170
- thiocyanate concentrations, smokers vs. passive smokers vs. nonsmokers, 1471
- thiocyanate levels in smokers vs. nonsmokers, 0213
- ureaplasmas, neonatal mortality and morbidity effects, with maternal smoking, 1051
- xenobiotic and steroid metabolism, cigarette smoking effect, 0211

PNEUMOCONIOSIS
(*See also* ASBESTOSIS; LUNG DISEASES)

coal miners, dust exposure and smoking as risk factors, 15-year followup, 1545
coal miners, lung function in smokers and nonsmokers, 1546

PNEUMONIA
(*See also* RESPIRATORY TRACT DISEASES)
infants, maternal smoking as factor, 1462
Legionnaires' disease, animal model for study, smoking effects on infection, 1497
lung defense mechanisms in patients, smokers vs. nonsmokers, 0378

POLONIUM-210
(*See also* METALS, METAL ISOTOPES; RADIATION)
distribution and clearance of alpha radioactivity in lungs of smoke-exposed rats, 1261

Polyphenols *See* **PHENOLS**

Population distribution *See* **DEMOGRAPHIC FACTORS**

PRECANCEROUS CONDITIONS
(*See also* NEOPLASMS)
atypias in sputum in high-risk smokers, 0764
atypical bronchial epithelial cells as markers for people at risk for lung cancer, 1461
Billroth II resection patients, lung cancer risk relationship, 0348
cervical dysplasia, sex behavior, oral contraceptive use, smoking in epidemiology, 0124
esophageal dysplasia screening of high-risk patients, 0856
leukoplakia in naswar (powdered tobacco) users in Pakistan, 0425
leukoplakia, malignant potential of tobacco-induced vs. idiopathic, 0165
metaplastic and dysplastic cells as evidence of epithelial process in squamous cell lung cancer, 0462
oral cancer risks in leukoplakia patients, 0262
oral conditions, smoking relationship from Israel survey, 1282
oral lesions in reverse smokers, 0065
oral lesions, tobacco use relationship in India, 0286
oral leukoplakia transformation, tobacco use as factor, 0714
reduction of lesions by stopping tobacco use, 0288

PREGNANCY
(*See also* EMBRYO; FETUS; NEONATE)
abortion, smoking, and other risk factors, 0772
adolescents, independent and dependent influences on health behaviors, 0657
adolescents, prenatal care effect on health behaviors during and after delivery, 0658
alcohol, nicotine, marijuana use before and during pregnancy in Canada, 0072
audiovisual slide presentation on health hazards of smoking, drinking, and medications, 0082
birth defects associated with drug abuse and smoking, 1043
blood vessels in umbilical cords, maternal smoking effects, 0184
breast feeding attitudes, smoking habit relationship, 0041
cadmium and zinc, interaction in smokers vs. nonsmokers, birth weight effect, 1345
cardiovascular, respiratory, and biochemical fetal responses to maternal smoking, 1228
cardiovascular response of mother and fetus to smoking, 0449
cessation of smoking, self-help vs. group therapy, efficacy, 0646
community reproductive care program, acceptability and efficacy, 0077
cotinine-assisted intervention to reduce smoking, birth weight effects, 0969
diabetic women, red cell oxygen transport and release, smokers vs. nonsmokers, 0156
diet, alcohol use, smoking, effects on lactation and infant growth, 1525
fetal and neonatal exposures, risk factors in infant gliomas, 1256
fetal carbon monoxide exposure, effect on brain neurochemical development, 1003
fetal effects of maternal coffee, alcohol, marijuana, and tobacco use, 1262
fetal heart rate variability, maternal smoking effect, 0202
genetically controlled responsiveness to hydrocarbons in mice, 0212
health risks of smoking, 0808
hemoglobin levels, birth weight, and smoking in normal pregnancy, , 0415
individualized counseling during obstetric care for smoking cessation, 1504
infant and child developmental effects of maternal tobacco, alcohol, and marihuana use, 0071
initiation of smoking by women after delivery, 0490
interagency smoking cessation program for pregnant women, 0634
intervention strategy for neighborhood prenatal clinics, 0713
intrauterine growth retardation, maternal factors, 0877
low birth weight and infant mortality, maternal smoking effect, 0419
low birth weight infants, maternal smoking effect, 0360
marijuana smoking, drug use, smoking, alcohol use, relationship with outcome, 1038
maternal alcohol consumption and smoking, effects, 0117
maternal alcohol use, smoking, and lead exposure effects, 1344
maternal O_2 transport at high altitudes, smoking effects, 0755
maternal smoking before, during, and 1 year postpartum, changes, 0073
maternal smoking effects, 0045
maternal smoking habits in France, trends 1972-1981, 0238
maternal smoking, National Survey of Family Growth, 0981
metallic mercury exposure effects, 0086
National Health Interview Survey, 1985 Supplement, maternal smoking, 0980
neonatal thyroid function, maternal smoking effects, 0423
nicotine and cotinine distribution and kinetics in pregnant sheep and fetus, 0672
nutrition, psychosocial stress, smoking effects on birth weight and length of gestation, 0555
nutritional status of pregnant women and risk factors for low birth weight, 0815
placental detoxification systems, response to maternal smoking, 0758
prenatal care and smoking as factors in risk of low birth weight infant, 1141
prenatal care program for reduction of premature births, efficacy, 0692

prostacyclin production, fibronectin synthesis, smokers vs. nonsmokers, 0322
spontaneous abortion, maternal smoking and other factors, 1257
steroidogenic enzymes of the feto-maternal-placental unit, effects of smoke constituents, 0392
teratogenic effect of chronic exposure to heavy metals (cadmium) in hamsters, 1164
thiocyanate concentrations in smokers vs. passive smokers vs. nonsmokers, 1471
underestimation of smoking by heavier smokers, 0545
ureaplasmas in placenta, mortality and morbidity effects, with maternal smoking, 1051
women at risk of small-for-date infants, factors with smoking, 0610
women in Norway, age, marital status, education effect on smoking habits, 0418
women under age 18, stress as factor in outcome, smoking relationship, 0652

PREMATURITY
intervention to reduce incidence, including smoking reduction, efficacy, 0692
maternal smoking effect, 0809

PREVENTION OF SMOKING
(*See also* ANTISMOKING CAMPAIGNS; HEALTH EDUCATION; SMOKING CONTROL PROGRAMS)
activity book on smoking and health for fourth and fifth grades, 0122
adolescents, efficacy of community involvement in program, 0729
adolescents in Israel, intervention program effectiveness, 0310
adolescents, school and community intervention program, 1421
adolescents, survey of factors influencing smoking initiation, 0716
adolescents, teacher-led vs. peer-led intervention program, efficacy, 1233
adolescents, value approach as coping strategy, 1541
age antismoking information was given, effects on smoking prevention, 0233
antismoking curriculum for grades 3 through 10 in Washington State, long-term followup, 1516
children aged 10 to 12, efficacy of education program, 0040
children aged 3 to 5 years, physician's program for prevention of smoking, 1476
children and adolescents in Manitoba, Canada, survey for program planning, 0081
children and adolescents in the Netherlands, educational program, 0398
children, health education for cardiovascular risk reduction, 1411
children in Australia, positive image of nonsmoker stressed, 0019
children in grades 4, 5, and 6, establishing antismoking attitudes, 1015
children, Primary Health Curriculum Project, followup study, 1524
culturally based model of tobacco use for development of strategies, 1173
district health authorities in England and Wales, policy recommendations, 0553
education program for fifth grade students in Moscow, 0502
fourth and fifth grade education program, mass media, parents as reinforcement, 1501
fourth graders, high school students as program leaders, 1217
health education for children aged 10 to 12, efficacy, 0589
health education programs, 0200
high-risk youth, efficacy of sixth grade curriculum, booster session effect, 1532
junior high school students, evaluation of two program approaches, 1213
junior high students, classroom television program with/without instruction, efficacy, 0724
Know Your Body program for grades 4-6, replication and evaluation, 0780
Latrobe Valley (Canada) community smoking control project, 4-year evaluation, 0079
life skills training, efficacy of maximum vs. minimum teacher support, 1235
Lifecycle model of preventive health services, factor in risk reduction, 1242
mass media campaign for adolescents, comparison of varied program content, 1323
media and community intervention programs in southwest Texas, 1481
Minnesota Heart Health Program, health education for seventh and ninth graders, 1135
multicomponent, multiyear school-based intervention project in Washington State, 1519
multidimensional antismoking program for seventh grade students, 0874
My Body program for primary school students in England, efficacy, 0568
peer-assisted education program for seventh grade in Canada, 0083
Primary Grades Health Curriculum Project vs. standard curriculum, efficacy, 1219
public policies, demography of smoking for designing and evaluating programs, 1070
review and critique of existing legal approaches to smoking control, 1047
Risk and Youth: Smoking Project in California elementary and junior high schools, 0675
school-based, skills training and health effects information for coping, 1550
school intervention programs for fifth and sixth grades, effectiveness, 1103
seventh grade programs, 0725
sixth grade curriculum development, Canada, 0127
sixth graders, peer leaders as teachers, 1364
skills training and health education in fifth and sixth grade, 1533
Smoke-Free Spaces for Kids, Canadian program to promote nonsmoking as the norm, 0069
students in Allegheny County, Pennsylvania, antismoking curriculum, 1383
students in grades seven and eight, experimental curriculum, evaluation, 1161
students in junior and senior high school, efficacy of anti-tobacco-chewing component, 1373
students in Moscow, effectiveness of intervention strategies, 0503

PROGRAMS AND POLICIES
(*See also* SMOKING CONTROL PROGRAMS)
American Cancer Society, California survey of smoking habits, attitudes, and beliefs, 0690
American Cancer Society FreshStart smoking cessation program, efficacy, 0688
American Lung Association, efficacy of smoking cessation clinics, 1218
American Lung Association Freedom From Smoking, efficacy, 0786
American Lung Association self-help smoking cessation program development for worksites, 1150
antismoking policies, Allegheny County (Pennsylvania) Health Department, 1382
antismoking program for military enlisted personnel in Italy, project components, 0334
antismoking programs and legislation in Egypt, evaluation of various approaches, 0173
Australian "Quit For Life," evaluation, 0009
British workplace programs for smoking cessation, attitudes of employees and employers, 0526
community program in Israel for reduction in smoking, 10-year followup, 0312
conferences to explore issues in smoking behavior research and policy development, 1068
education program for smoking prevention in fifth grade students in Moscow, 0502
Finland, economic simulation model for analyzing options, 0199
four-phase media campaign to promote smoking cessation in Western Australia, efficacy, 0015
Framingham Offspring Study, Cycle III, 1041
health districts in England and Wales, smoking prevention/cessation policies, 0553
high school designated smoking area, effect on smoking incidence, 0611
hospital antismoking policy formation and implementation, 1072
hospitals in Australia, smoking control policies, 0011
Institute for the Study of Smoking Behavior and Policy, Harvard University, 1069
Kaiser-Permanente risk reduction program for members, efficacy for smoking and stress, 0642
Lifecycle model of preventive health services, Metropolitan Life Insurance Co., 1242
Minnesota Heart Health Program, community-based interventions, 1135
MONICA, monitoring trends and determinants of cardiovascular diseases, 0059
multifaceted program in Israel for smoking prevention/cessation, 0304
National Cancer Institute telephone communication network for smokers who want to quit, 1307
no smoking policies in workplaces, economic benefits, 1279
Operation Smokestop (England), community-based self-help network for cessation, 0576
Pan American Health Organization, cessation/prevention programs in Texas, 1481
PASS UP, parents and students substance use prevention, efficacy for seventh graders, 0726
Pennsylvania Department of Health, antismoking education project, 1395
policy alternatives in smoking and health controversy, 0789
Primary Grades Health Curriculum Project vs. standard curriculum, efficacy, 1219
Project Smart (Los Angeles), drug abuse intervention program for adolescents, efficacy, 0727
Project VOTE, Kansas program to promote workplace smoking policy, 0876
restraints on smoking and cigarette promotion in New Zealand, public attitudes, 0403
restricted smoking area in office building, effect on general air quality, 0068
Second International Study of Infarct Survival, 0547
Smoke-Free Spaces for Kids, Canadian program to promote nonsmoking as the norm, 0069
tobacco industry control, simulated effects of policy changes, 1319
Trades Union Congress in England, workplace program in response to resolution on smoking, 0523
World Health Organization, survey of attitudes and practices, smoking in hospitals, 0010

PROSTAGLANDINS
cultured umbilical vein cells, maternal smoking effect on prostacyclin production, 0322
nicotine and smoke exposure effects on formation, 0452
prostacyclin and thromboxane production in smokers vs. nonsmokers, 1458
prostacyclin release from arterial cells, smoking and oral contraceptive use effects, 0321

PROSTATE
hypertrophy, risk factor for bladder cancer, 0164
reduced size in smoking dogs, 1186

PROSTATIC NEOPLASMS
Nebraska Laboratory Cancer Research Center, objectives, 1154

PROTEIN CONTENT
cured tobacco leaf, extraction techniques, 0949
reduction to produce safer smoking material, 1032
soluble protein removal and carcinogenicity, 0603

PROTEINS
(*See also* AMINO ACIDS; LIPOPROTEINS)
albumin as biochemical marker in chronic obstructive pulmonary disease, 1296
albumin, determination of carcinogen-protein adducts for estimating human exposure, 1077
ceruloplasmin and ferrous iron transferrin, roles in chronic obstructive pulmonary disease, 1297
fibronectin synthesis by cultured umbilical vein cells, maternal smoking effect, 0322
glycoprotein, alterations in biosynthesis in murine cells exposed to sidestream smoke, 0937
interferon induction in male lung cancer patients, smoking effect, 0609

keratins, effect of tobacco smoke components on expression in vitro, 0157
NAD(P) glycohydrolase as acidic protein, properties and mechanisms of action, 1050
phenotypic analysis of epithelial cell neoplastic progression, biosynthesis, 1507
phenytoin and propranolol, protein binding in serum, smoking effect, 0899
plasma levels, cigarette smoking effect on complement and control proteins, 0907
polycyclic hydrocarbon binding to cytosolic protein in carcinogenesis, 1156
respiratory tract glycoproteins, markers of susceptibility to lung disease, 0769
serum albumin levels, oral leukoplakia relationship, 1459

PSYCHIATRIC DISORDERS
(*See also* NEUROTICISM)
cancer mortality in psychiatric patients, smoking relationship, 0388
depression in smokers vs. nonsmokers, 0686
determinants of early mortality in patients, 1095
expression of anger in group psychotherapy, smoking prohibition effects, 1301
sodium-dependent lithium efflux in diagnosis, tobacco use as physiologic influence, 0837
tobacco smoking as coping mechanism in patients, 0098

PULMONARY ALVEOLAR MACROPHAGES
(*See also* MACROPHAGES; PHAGOCYTOSIS)
arachidonate lipoxygenase products, release in smokers in lung disease etiology, 0919
benzo(*a*)pyrene metabolism in baboons, chronic vs. novice smokers, 1467
chronic tobacco smoke exposure effects in rat lung, 0801
elastase activity in lavage fluid from upper vs. lower lobes, 0114
elastase secretion, urinary desmosine as indicator, 1147
elastolytic activity in current smokers vs. ex-smokers, 0302
emphysema relationship in hamsters, 1450
interaction with human neutrophil elastase, 1044
interleukin-1 production, response to lung infection and smoking, 1165
leukotriene D_4 receptors, smoking and nicotine effects, 1153
levels in smoke-exposed macaques and controls, 1446
lungs of young and old mice, response to long-term smoke inhalation, 0895
metabolic effects of cigarette smoke, 0338
morphologic and functional characteristics in smokers vs. nonsmokers, 0802
neutrophil elastase activity in disease etiology, 1140
occupational air pollution and smoking, synergistic effects, 0421
population size, cell dimensions, and ultrastructure in mice, smoke inhalation effects, 0896
sarcoidosis patients vs. smokers vs. nonsmokers, 1415
superoxide production, chronic and acute effects of smoking, 0112
surface cell marker correlation with immunoregulatory function in smokers, 0180
synergistic effect of cigarette smoke and silica dust, 0475
tumoricidal potential, smoking effect, 0803

PULMONARY ALVEOLI
antibody production to inhaled antigens in allergic alveolitis, smoking effect, 0585
epithelial permeability, experimental study with 99^{Tc}-DTPA in smokers, 0060
high-fat diet and smoke effects on lung tissue morphology in monkeys, 0868
nitrogen dioxide and ozone, long-term exposure effects in monkeys, 0653
permeability and edema in smoke-exposed rabbits, 0620

PULMONARY CLEARANCE
(*See also* CILIARY ACTIVITY; LUNG FUNCTION; RESPIRATORY FUNCTION TESTS)
aerosolized technetium-labeled diethylenetriamine pentacetic acid in smoke-exposed rabbits, 0620
chronic bronchitis patients, smokers vs. ex-smokers, 0550
developmental age effect on deposition and clearance of inhaled particles, 0854
nonsmokers vs. asymptomatic smokers, clearance of 99^{Tc}-DTPA, 0060
polystyrene particles, deposition and clearance in smokers vs. nonsmokers, 0551

Pulmonary diseases *See* LUNG DISEASES

Pulmonary emphysema *See* EMPHYSEMA

PULMONARY FIBROSIS
(*See also* LUNG DISEASES)
alveolar macrophages, clinical and pathophysiological relationship, 1499
changing patterns of damage in long-term smoke-exposed dogs, 1178
organ, tissue, and cell analyses to determine etiologic agents, 1498
tar and nicotine levels in smoke-exposed dogs, relationship, 1180

Pulmonary function *See* LUNG FUNCTION

PULMONARY HEART DISEASE
(*See also* HEART DISEASES)
occupation, environment, and smoking as risk factors, 0275

Race factors *See* ETHNIC GROUPS

RADIATION
(*See also* LEAD; POLONIUM-210)
brain tumors in children and adolescents, risk factor with passive smoking, 0733
cancer mortality in uranium miners, exposure and smoking as factors, 0242
cigarette smoke interaction with radon daughters in uranium miners, 1492
dental x-ray and other exposures, effect with smoking on parotid gland cancer, 0721
head and neck cancer patients, radiotherapy effect on carcinoembryonic antigen titer, 1185

mastectomy patients, coronary artery disease and secondary malignancies, relationship, 1067
plutonium aerosols on tobacco grown near chemical plant, potential dose, 1443
plutonium, cancer and disease risk in exposed workers, smoking effect, 1187
plutonium in respiratory tracts of rats and dogs, smoke inhalation effect, 1515
radon and radon daughters in dwellings, effect on lung cancer etiology, with smoking, 0453
radon decay products on smoke tar particles, bronchial deposition, 0752
uranium miners in Canada, mortality risk factor, with smoking, 0097
uranium miners radon daughter exposure, effect with smoking on lung cancer incidence, 1189

RECIDIVISM
(*See also* CESSATION OF SMOKING; WITHDRAWAL CLINICS)
attitudes and beliefs as factors, 0525
behavior modification and a "buddy" system for reduction, 1401
behavioral conditioning and nicotine gum in prevention, 0703
carbon monoxide feedback in group cessation program, effect at 6, 12, 18 months, 0786
causal attributions by initially abstinent clinic participants, 1368
cessation abstinence vs. relapse, factors, 1094
demographic characteristics of relapsed quitters, 1070
everyday stressors as factors in relapse, 0799
followup letters to maintain abstinence, effectiveness, 1337
health and self-efficacy beliefs as factors, 1457
Minnesota quit smoking contest, predictive factors, 1122
nicotine gum and coping skills training, effect, 0659
nicotine gum, prevention efficacy, 0662
Normative Aging Study in middle-aged men, factors, 1046
nurses in Minnesota, reasons for quitting and factors in relapse, 1124
physician's advice on cessation, 6-month and 12-month rates, 0120
predictive factors, sex-related differences, 0655
prepaid medical plan smoking cessation program, attendance as factor, 0643
prevention as part of smoking cessation program, 1300
psychological characteristics in relapsers vs. ex-smokers vs. nonsmokers vs. smokers, 1349
recovering alcoholics, characteristics vs. successful quitters, 1527
relapse episodes, cluster analysis and prediction of relapse situations, 1376
relapse factors in long-term maintenance of cessation, 1089
restricted environmental stimulation therapy for reduction, with behavioral modification, 0109
self-efficacy score at quitting as predictor of relapse, 0046
self-help cessation of smoking, motivation as factor vs. successful quitters, 1065
self-quitters, characteristics vs. continuing abstainers, 0666
self-quitters, efficacy of relapse prevention hotline, 1289
skills training for quitters, effectiveness at 12-month followup, 1367
social background, type of smoker, family environment as factors, 1031
social network members, influence, 1162
social skills training for prevention, efficacy, 0794
variables associated with cessation, maintenance, and reinitiation, 1142
worksite cessation program participants, factors, 0691

Reconstituted tobacco *See* TOBACCO, RECONSTITUTED

Rectal neoplasms *See* INTESTINAL NEOPLASMS

RECTUM
nicotine self-administration in dogs, effect on temperature, 1013

REDUCTION OF SMOKING
(*See also* CESSATION OF SMOKING; WITHDRAWAL CLINICS)
angina patients in minimum-contact intervention program, 1496
behavior modification cessation program, effect on short- and long-term quit rates, 1085
clonidine, aminophylline, and propranolol effects on cigarette consumption, 1506
clonidine effectiveness in reducing smoking, 1488
goal of smoking control program, effectiveness compared with cessation, 1336
gradual withdrawal program for smoking cessation, efficacy, 0836
group cohesiveness in cessation program, effect on reduction, 1547
head and neck cancer patients, reduced risk for second primary cancer, 0715
health and self-efficacy beliefs as success factors, 1457
hypnosis and fading procedure, effectiveness, 1325
letters following smoking cessation treatment, effectiveness, 1337
monetary payments, efficacy, 1008
myocardial infarct patients, rehabilitation program efficacy, 0399
patients and hospital employees, comparison of three programs, 1426
pregnant women, cotinine-confirmed intervention program, efficacy, 0969
pregnant women, for reduced risk of premature births, 0692
review and critique of existing legal approaches to smoking control, 1047
social network members, influence, 1162
three-stage program, effectiveness, 1149
worksite competition-based program, efficacy, 1339
worksite smoking cessation program, effectiveness, 1371

RESPIRATORY FUNCTION TESTS
(*See also* LUNG FUNCTION)
adolescents in health education for smoking cessation, effectiveness as tool, 0330
adolescents, smoking-induced changes in ventilation, diffusing capacity, capillary volume, 0328
aerosol particle distribution in smokers vs. nonsmokers, 1260
age, sex, height, and race effects in adolescents in Tahiti, 0497
air crewmen, coronary disease risk factor determination, 1465
air pollution effects in smokers vs. nonsmokers, 0682
airways responsiveness in adults, smoking effect, 1096
alcohol consumption in smokers, inflammatory response suppression, 0913
asthmatic children, passive smoking effects, 0076
asymptomatic middle-aged male smokers, predictive value, 0223

SUBJECT INDEX

athletes in various sports, smokers vs. nonsmokers, 0316
bakers, lung disease risk factors determination, 0248
bronchial cancer patients, smoking effect, 0101
children aged 6 to 12, effect of parental smoking and gas cooking, 0870
children and adolescents, automated computation, 0222
children, environmental exposures and passive smoking effects, 0049
chronic airflow obstruction, predictive value, 1370
chronic pulmonary disease intervention/prevention, smoking cessation effects over time, 1127
coal miners exposed to diesel fumes, smoking effect, 1544
environmental factors in reduced function, smoking relationship, 0618
firemen, changes over time, occupational exposure and smoking as factors, 0509
healthy smokers vs. nonsmokers, mechanisms of obstructive airways disease, 0619
insurance company employees, spirometry in health promotion program, 1448
iron miners, changes over 5 years in smokers vs. nonsmokers, 0221
"lung age" estimation for motivating smoking cessation, 1381
lung cancer screening program for steel workers, smoking effect, 0635
lung function changes in smokers, efficacy of simple tests, 0279
male smokers, early detection of airway disease, 0514
medical students aged 19 to 25, changes over 3 years, 0166
middle-aged males in MRFIT trial, long-term followup, 1419
neon vs. air inhalation effects on spirometry to detect COPD, 0633
nonsmokers, asymptomatic smokers, symptomatic smokers, response to methacholine, 0277
nonsmokers, effect of moderate and heavy cigarette smoke exposure, 0126
nonsmokers vs. smokers before and after smoking one cigarette, 0363
occupational disease risks, smoking relationship, 0017
passive smoking effects in nonsmokers, 0018
pediatric, long-term consequences of childhood airway diseases, 0617
poultry workers, dust exposure and smoking effects, 0465
reduced minute ventilation in animals exposed to cigarette smoke, 0479
sarcoidosis patients, smokers vs. nonsmokers, 0094
serum protein and ceruloplasmin levels in smokers, relationship, 0907
spirometry in adolescents, smoking habit relationship, 0240
subjective and objective measurement of smoke inhalation, disease severity relationship, 0791
symptomatic smokers, airway reactivity following cessation, 1271
transit time analysis of forced expiration after H_2O mist exposure in smokers, 0329
ventilatory capacity, predictor of lung function changes over 13 years, 0434

RESPIRATORY SYMPTOMS
(*See also* COUGH)
adolescent smokers, tool for antismoking campaigns, 0226
adolescents in France, smoking habit relationship, 0240
adolescents in Tahiti, smoking habit relationship, 0497
adolescents, relationship with smoking, 0305
air pollution, socioeconomic status, smoking as factors in India, 0293
alveolar hypoxia relationship to ventilatory control disorders, 1138
apnea and hyperpnea in smoke-exposed awake dogs, nicotine level effect, 0917
bakers, lung disease risk factors determination, 0248
blue collar workers, smoking relationship, 1543
cessation of smoking effect, 0689
children, air pollution and passive smoking effects, long-term followup, 0435
children, gas cooking and parental smoking as factors, 0870
children, parental smoking association, 1105
chronic bronchitis subjects who smoke, effect of ozone exposure, 1024
females in Hong Kong, lung cancer risk factors, 0258
hospitalized patients, relationship with occupation, residence, and smoking history, 0519
medical college students in India, smoking habit relationship, 0263
middle-aged cohort in western Scotland, passive smoking as factor, 0591
nonsmokers exposed to moderate and heavy cigarette smoke, influence of suggestibility, 0126
occupational air pollution exposure and smoking, synergistic effects, 0421
prevalence in smokers vs. ex-smokers vs. nonsmokers, 0560
questionnaires as screening instruments in asbestos workers, 0460
snow crab processing workers, factor with smoking in occupational asthma, 0084
sulfur dioxide-exposed workers, smoking as factor, 1061
women vs. men, cigarette consumption effect, 0234

RESPIRATORY SYSTEM
(*See also* BRONCHI; BRONCHIOLES; LARYNX; LUNGS; TRACHEA)
acute effects of inhaled cigarette smoke in awake dogs, 0917
airway reactivity and frequency-dependent compliance to cigarette smoke in lambs, 0793
airway reactivity, smoking cessation effect in symptomatic smokers, 1271
airway receptors, response to cigarette smoke and nicotine aerosols, 0893
airway smooth muscle, nicotine effect on leukotriene D_4-induced responses, 1153
airways inflammation, smoke-induced in guinea pigs, mechanisms, 0108
asbestos workers, exposure-related abnormalities, smoking as factor, 0096
body mass index and physical activity, effect in smokers vs. nonsmokers, 0252
bronchial responsiveness to methacholine, smoking effect, 0391
chemosensory stimuli produced by cigarette smoke, 0693
chronic airflow limitation and blood vitamin C levels, smokers vs. nonsmokers, 0125
chronic airflow obstruction, predictive value of function tests, 1370
clearance rate of dust in smokers vs. nonsmokers, 1076
cytopathological, cytochemical, and prospective studies of smokers, 0462

SUBJECT INDEX

deposition and clearance of inhaled polystyrene particles, nonsmokers vs. smokers, 0551
diurnal variations in airway obstruction in asthmatics and bronchitics, smoking effect, 0512
epithelioid cells and adenovirus types 5 and 7, in vitro smoke effects, 1169
experimental smoking conditions, responses in humans and rabbits, 0371
morphologic changes in smoke-exposed dogs, emphysema relationship, 1179
neutrophil elastase activity in disease etiology, 1140
nicotine injection and smoke inhalation effects in cats and monkeys, 0265
nonspecific airway reactivity, smoking relationship in bronchial cancer patients, 0101
oxygen consumption during exercise, smokers vs. nonsmokers, 0601
plutonium retention and distribution in rats and dogs, smoke inhalation effect, 1515
rats, smoking-induced alterations, measurement, 0480
surgery patients who smoke, presurgery abstinence effect, 0513
ventilatory response to hypercapnia in dogs after intravenous nicotine injection, 0389
ventilatory response to hypoxia in twin pairs smokers vs. nonsmokers, 0365

RESPIRATORY TRACT DISEASES
(*See also* BRONCHIAL DISEASES; EMPHYSEMA; LUNG DISEASES)
acute decompensation in adolescents smoking clove cigarettes, 0106
adenoviruses in etiology, in vitro smoke effects on types 5 and 7, 1169
adolescents in Tahiti, smoking habit relationship, 0497
carboxyhemoglobin levels in patients, calculated vs. measured in smokers, 0075
child at age 10, parental smoking relationship, 1192
childhood, long-term effects with other risk factors, 0617
children and young adults, air pollution and passive smoking effects, long-term followup, 0435
children, gas cooking and parental smoking as factors, 0870
chronic airflow limitation in smokers vs. nonsmokers, blood vitamin C levels relationship, 0125
chronic disease in wives of smokers, passive smoking as factor, 0280
diet, socioeconomic status, and smoking as factors in Indian adults, 0292
Hispanics vs. whites, smoking habit relationship, 1190
hospitalized patients, effect of advice on smoking cessation, 0130
mortality, air pollution, smoking, ionizing radiation as factors, 1410
mortality, smoking, air pollution, occupational exposure as risk factors, 13-year followup, 0434
occupational hazards and smoking relationship, 0017
plant workers in Czechoslovakia, incidence in smokers vs. nonsmokers, 0153
reverse (chutta) smoking effects, 0276
tuberculosis patients given isoniazid, lung cancer risk with smoking, 0508

RESPIRATORY TRACT INFECTIONS
(*See also* BRONCHITIS; PNEUMONIA)
adolescents smoking clove cigarettes, possible chronic and acute effects, 0106
child at age 10, parental smoking relationship, 1192
infants, parental smoking as risk factor for viral infections, pneumonia, 1462
interleukin-1 production, response to lung injury, with smoking, 1165
Legionnaires' disease, animal model for study, smoking effects on infection, 1497
syncytial virus infection in infants, long-term effects, parental smoking as factor, 1287

RESPIRATORY TRACT NEOPLASMS
(*See also* BRONCHIAL NEOPLASMS; LUNG NEOPLASMS; NOSE NEOPLASMS; TRACHEAL NEOPLASMS)
benzo(*a*)pyrene-induced in hamsters, vitamin A intake effect, 0396
etiology, tobacco and other environmental factors, 0858
males in Egypt, increasing incidence, 0173
mortality, smoking relationship, 0971
occupation, education, diet, alcohol consumption, and smoking as factors, 0665
occupational/residential formaldehyde exposure as factor, 1518
tobacco smoke as causative factor, data analysis of European countries, 0244

REVERSE SMOKING
(*See also* SMOKING)
beta-carotene for prevention of oral lesions and carcinomas in users, 0065
chronic bronchitis and respiratory function impairment, length of habit relationship, 0281
lung function and morbidity, effect of chutta smoking, 0276
oral cancer relationship in Colombia, 0150

Retinitis *See* **EYE DISEASES**

Rhinitis *See* **RESPIRATORY TRACT INFECTIONS**

Ribonucleic acid *See* **RNA**

RNA
(*See also* DNA)
benzo(*a*)pyrene effects on levels in pancreatic tissue, 0827
epoxide hydrolase mRNA in rat liver, role in carcinogenesis, 1157
^{3}H-dibenzo(*c, g*)carbazole binding, 1359
nitrosamines in tobacco smoke administered to nursing rats, effects in sucklings, 0001

SALIVA
immunoglobulin levels in 13-year-olds, smokers vs. nonsmokers, boys vs. girls, 0437
N-nitrosamines, determination, 1404
N-nitrosamines, formation in areca chewers, 1196
smokeless tobacco extracts, interactive effect in periodontal disease etiology, 1029
tobacco components, levels as indicators of oral cancer risk, 1184

SUBJECT INDEX

SELENIUM
blood and serum levels in smokers vs. nonsmokers, 0578
blood levels, effect of age, alcohol consumption, smoking, oral contraceptives, 0577
serum level, smoking relationship, 1001
tissue levels as cancer test and biological implications, 0751

SEROTONIN
brain receptors, smoking effect, 0584
serum levels in dogs, nicotine injection effect, 0377

SEX BEHAVIOR
(*See also* BEHAVIOR, HUMAN; BEHAVIOR, ANIMAL)
abstinence from smoking, attitudinal factors in males vs. females, 0525
arousal in vascular disease patients, smoking effects, 1440
arousal in women, smoking effects, 1439
dysfunction, smoking habit relationship, 0315
Mormons, cervical cancer relationship, 1491
similarities and differences in smoking in males vs. females, factors, 1166
women, cervical dysplasia risk relationship, with smoking, 0124

SEX RATIO
(*See also* WOMEN)
adolescents and adults in New Zealand, changes in smoking habits, 1976 vs. 1981, 0404
adolescents in Great Britain, smoking initiation factors, 0505
adult smokers in the United States, 1982 survey, 0816
adult smoking habits in Italy, trends since 1900, 0331
adults in Ireland, social and cultural influences on smoking behavior, 0295
alcohol consumption, smoking, and drug use among high school students in Italy, 0342
arteriosclerotic lesions, smoking as risk factor, 0172
cancer mortality in Poland, demographic and epidemiologic factors, 0433
cancer mortality, variations in risk factors, 0231
changing smoking patterns in Finnish university students, 0208
children and adolescents in Perth, Australia, smoking habits, 0012
chronic bronchitis vs. airways obstruction, risk relationship, 1005
cost benefit of smoking cessation, age and amount smoked as factors, 1079
doctors, teachers, athletes, armed forces members in Egypt, smoking habits, 0173
duodenal ulcer, attributable risk in smokers, 0650
electroencephalogram response to nicotine, 0744
hemodynamics in healthy smokers vs. nonsmokers, age effects, 0602
immunoglobulin levels in 13-year-olds, smokers vs. nonsmokers, 0437
life stress levels as predictors of smoking cessation success, 1108
longevity, smoking effect, 1402
longevity in nonsmokers, 1397
lung cancer, adults in Shanghai, smoking-related risks, 0142
lung cancer growth rate, 0319
lung cancer in Japan, differences in development and growth, 0349
lung cancer mortality in Switzerland, age as factor, 0495
lung cancer risk in Hispanics vs. whites, smoking as factor, 1191
lung function and smoking habits of adolescents in Sydney, Australia, 0044
lung function decline, peripheral airways obstruction as predictive factor, 0105
mortality risk factors in urban and rural areas of Shanghai, 0145
motives for smoking based on adolescent personality measures, 0674
Napa Drug Abuse Prevention Project, findings of school-based programs, 0647
oral cancer incidence in Colombia, smoking and reverse smoking relationship, 0150
pancreatic cancer relationship in adult smokers, 1390
personality correlates in long-term smokers vs. nonsmokers vs. ex-smokers, 0670
recidivism at 12 months following smoking cessation, predictors, 0655
smokeless tobacco use and smoking, junior high school students in Wyoming, 1561
smokeless tobacco use by college undergraduates, 0844
smokeless tobacco use by high school students in Arkansas, 0625
smoking and smokeless tobacco use in the elderly, 0796
smoking habits in Australia, 0009
smoking habits of adults in Norway, 10-year changes, 0408
smoking-related respiratory symptoms in men vs. women, 0234
snuff use by adolescents in Sweden, oral health relationship, 0456
students aged 12 to 18 in Utah, smoking and smokeless tobacco use patterns, 1495
students in grades 7 through 12 in Ohio, smoking habits, changes over time, 1341
urinary excretion of D-glucaric acid in smokers, 0340
Veterans Administration Medical Center employees, smoking habits, 0970
youths and adults in rural community of Nepal, smoking habits, 0393

SKIN
benzo(*a*)pyrene, asymmetric interactions with DNA, 1102
capillary blood flow, cigarette nicotine content effect in smokers, 0914
DNA adducts analysis method for carcinogens, 1460
hypersensitivity in noise-exposed workers, 0438
permeability to nitrosonornicotine, with/without ethanol, 0875

SKIN DISEASES
dermatitis, nicotine as allergen, 0217
idiopathic systemic lupus erythematosus, risk factors, 1413
psoriasis patients, absorption of mutagens from crude coal tar, 0743
seborrhoeic dermatitis, nicotine as hapten in etiology, 0247

SKIN NEOPLASMS
(*See also* CARCINOMA, EPIDERMOID)
malignant melanoma, heavy cigarette smoking as adverse factor in prognosis, 1073

SLEEP
withdrawal symptom following smoking cessation, 0026

SUBJECT INDEX

SMALL AIRWAYS DISEASE
  (*See also* OBSTRUCTIVE AIRWAY DISEASES; RESPIRATORY TRACT DISEASES)
  acoustic energy response technique in diagnosis, 0840
  audible sound transmission for detection, 0965
  obstruction as predictor of lung function decline, sex and smoking as factors, 0105
  smoke-induced in guinea pigs, induction mechanisms, 0108
  trypsin and elastase inhibitory capacity relationship, smoking effect, 0906

Smell *See* **NOSE**

Smog *See* **AIR POLLUTION**

Smoke, bidi *See* **BIDI SMOKE**

Smoke, cigarette *See* **CIGARETTE SMOKE**

Smoke condensates *See* **TARS, CIGARETTE; TARS, TOBACCO**

SMOKE INHALATION, ANIMAL
  (*See also* SMOKING; TOBACCO SMOKE)
  acute respiratory effects in awake dogs, nicotine level effect, 0917
  adhesion and diapedesis of mononucleated cells in rats, effect, 1090
  aerosolized technetium-labeled diethylenetriamine pentacetic acid clearance in rabbits, 0620
  airway reactivity and frequency-dependent compliance in lambs, 0793
  airway receptors, response vs. nicotine aerosols, 0893
  airways inflammation in guinea pigs, induction mechanisms, 0108
  antioxidant activity of red blood cells, effect, 0759
  arachidonate metabolism in rats, effects, 0918
  arterial blood pressure regulation effects in rats, 0904
  arterial endothelium in rats, effects, 0535
  arteriosclerosis, physiological and biochemical effects in rabbits, 0372
  atherogenic effects in hamsters, 1203
  automatic, continuous aerosol generating and exposure system, smoke mixing capability, 1264
  automatic, programmable, continuous smoke exposure system, 1263
  biochemical defense mechanisms in exposed rats, 0889
  bone marrow production of inflammatory cells and precursor stem cells, effect in mice, 0886
  bronchial cancer formation in hamsters, carbon filter effect, 0175
  cardiomyopathy effects in rabbits, 0155
  cardiovascular and pulmonary function effects in rabbits, 0370
  cardiovascular effects in monkeys and cats, 0264
  cardiovascular, respiratory, psychomotor responses in rabbits, 0371
  cellular and subcellular effects in neonates of rats, 0778
  chronic exposure effects in macaques, 1446
  cytolytic functions of pulmonary effector cells, effects in mice, 0903
  d-nicotine in rats and mice to measure degree of racemization of l-nicotine, 0760
  degenerative changes in intervertebral discs in rats, 1500
  dietary antioxidant effect on smoke toxicity and carcinogenicity in hamsters, 0367
  duodenal mucosal blood flow, effects in rats, 0748
  elastase-induced emphysema in hamsters, effects, 1226
  emphysematous changes in rat lung, effect with porcine pancreatic elastase, 0900
  endocrine function disturbances in male and female rats, 0454
  fibrinolysis in rats, effect with injections of contraceptive hormones, 0451
  high-fat diet and smoke effects on lung tissue morphology in monkeys, 0868
  histamine and serotonin levels in guinea pig plasma, effect, 0377
  immune response in rats, effects, 0915
  improvement and monitoring of smoke generating, manipulating, and exposure systems, 0894
  interferon production effects in mice, mainstream vs. sidestream, 0939
  leukocytes and alveolar macrophage elastase, effect on rat lung, 1117
  lung function, synergistic effect of smoke and silica dust, 0475
  lung permeability in smoke- and elastase/smoke-exposed hamsters, 1119
  mask and smoke dosage apparatus for inhalation studies in rabbits and small rodents, 0368
  microcirculation in brain of bullfrogs, effects, 0364
  neuroendocrine cell innervation in neonates of smoke-exposed hamsters, 1555
  nicotine binding density, effect of chronic exposure in rats, 0910
  nitrosation potential of inhaled cigarette smoke in mice, rats, hamsters, 1208
  platelet thrombosis and clotting, coronary artery disease relationship, 1554
  plutonium retention and distribution in respiratory tract of rats and dogs, effect, 1515
  polonium-210 in cigarette smoke, distribution and clearance of radioactivity in rat lung, 1261
  prostacyclin and thromboxane alterations in exposed rats, 0890
  proteoglycan catabolism in bronchoalveolar lavage of baboons, smoking effect, 0962
  pulmonary alveolar macrophages in rats, chronic exposure effects, 0801
  pulmonary and cardiovascular effects of long-term smoke exposure in dogs, 1178
  pulmonary macrophage response in young and old smoke-exposed mice, 0896
  pulmonary metabolism of arachidonic acid, effect in rats and hamsters, 0214
  pulmonary tissue response to long-term inhalation in young and old mice, 0895
  respiratory effects in cats and monkeys, 0265
  respiratory system effects in dogs, emphysema relationship, 1179
  respiratory tract alterations, smoking product identification, 0480
  sidestream smoke vs. mainstream smoke, carcinogenicity in hamsters, 1209
  spicules in rat lung, structure, interrelationships, chemical identity, 1343
  tar and nicotine levels, pulmonary and cardiovascular effects, 1180
  thromboxane and prostaglandin synthesis, effects, 0452
  uterine blood flow and catecholamine response in pregnant ewes, 0671

vascular reactivity and arrhythmogenic threshold changes in rats, 0912
ventilatory function in rats following exposure, 0479

SMOKE STREAMS
aging effects on smoke nicotine and particulates content, 0267
analysis methods for sidestream smoke, IARC report, 0250
aryl hydrocarbon hydroxylase and dimethylnitrosamine demethylase, effects of smoke, 0343
carbon monoxidase for detection and conversion of carbon monoxide, 1303
carcinogens in sidestream smoke, inhibition of localization in epithelial tissues, 0935
cigarette smoke components, distribution ratio in sidestream and mainstream smoke, 0374
glycoprotein and polypeptide biosynthesis in murine cells exposed to sidestream smoke, 0937
interferon production effects in tissue cultures and mice, mainstream vs. sidestream, 0939
mainstream smoke, effect on cytolytic functions of pulmonary effector cells in mice, 0903
multicomponent characterization of mainstream and sidestream smoke, methodology, 1447
N-nitrosodiethanolamine levels in tobacco products, 1197
radon decay products in mainstream smoke, bronchial deposition, 0752
sidestream smoke as source of nitrosamines in indoor air pollution, 0387
sidestream smoke carcinogenicity in animals and humans, 1209

SMOKELESS TOBACCO
buccal mucosal effects in hamsters, 1058
elderly persons, use in blacks vs. whites, males vs. females, 0796
naswar, powdered tobacco product used in Pakistan, oral cancer risk, 0425

Smoke, tobacco *See* **TOBACCO SMOKE**

SMOKELESS TOBACCO USE
Current Population Survey, questions in September 1985 and 1986, 0973

SMOKING
(*See also* BIDI SMOKING; CIGARETTE SMOKE; CIGAR SMOKING; MARIJUANA SMOKING; MATERNAL SMOKING; OPIUM SMOKING; PARENTAL SMOKING; PATERNAL SMOKING; PIPE SMOKING; SMOKE INHALATION, ANIMAL; SNUFF-DIPPING; TOBACCO CHEWING)
biochemical markers and behavioral measurements of β-endorphin effects on reinforcement, 0767
breath luminescence effect, 1409
cancer risk relationship, with alcohol consumption and diet, long-term study, 1275
chronic illness and absenteeism relationship, with social class and age, 0543
conferences to explore issues in smoking behavior research and policy development, 1068
Current Population Survey, national sample and prevalence estimates, 0973
demography, designing and evaluating public policies for cessation or prevention, 1070
economic costs in Finland, 0199
hospitals, attitudes and practices worldwide, WHO survey, 0010
Institute for the Study of Smoking Behavior and Policy, Harvard University, 1069
international collaborative study of lung cancer risk, 0228
lung cancer risk relationship, with airways obstruction, 1006
morbidity and mortality in the United States, 0810
Normative Aging Study in middle-aged men, longitudinal effects, 1046
public policy alternatives in smoking and health controversy, 0789
review article on immune system effects, 0431

Smoking behavior *See* **BEHAVIOR, HUMAN; SMOKING CHARACTERISTICS**

Smoking, bidi *See* **BIDI SMOKING**

SMOKING CHARACTERISTICS
alcohol withdrawal effects, 1302
bladder cancer, risk relationship, 1010
blood concentrations of smoke constituents, relationship, 0905
brand switchers, changes, 0533
butt length with hypnosis reduction program, 1325
cigarette yield effects, 0806
compensatory puffing characteristics in smokers of low-yield brands, 0522
health practices, food habits, personality, and social factors, 0350
high- vs. low-tar cigarettes, inhalation pattern changes, 0792
hospitalized alcoholics, puffing patterns following smoking restriction, 1427
inhalation and puffing patterns in adolescents and adults, 0705
inhalation patterns in Greek adolescent smokers, 0251
inhalation patterns, lung disease relationship, 0489
inhalation practices and risk of myocardial infarct and cancer, 1299
inhalers vs. noninhalers, deprivation effects on tidal CO boost and pulse rate, 0487
Japanese junior high school students compared with U.S. data, 0351
light vs. deep inhalers, nicotine utilization for stress reduction, 0483
lip pressure and filter coverage, importance in designing smoking machines, 0846
lung cancer etiology, effect in Bangladesh, 0051
nicotine preference following deprivation or satiation, 0737
pharmacological and behavioral variables, effects, 0992
puffing and inhalation patterns in adolescent and adult marijuana smokers, 0706
puffing and inhalation patterns under different levels of stress, 0481
puffing behavior, personality and consumption correlates, 0485
puffing patterns, effect of control over tar delivery, 0693
rapid smoking in cessation program, cardiac response as abstinence predictor, 1553
rate variation in response to drug administration, 1012
rural African population, effect on esophageal cancer incidence, 0445

sedative vs. stimulant smokers, perceived stress and arousal as factors, 0561
topographic analysis of smoking behavior, laboratory vs. natural environment, 1125

SMOKING CONTROL PROGRAMS
corporate smoking policies, review of implementation process, 1047
hospital programs for employees and patients, 0968
hospitals in Victoria, Australia, 0011
North Karelia Youth Project for students aged 12 to 16, 0200
positive vs. neutral feedback and cessation vs. reduction, comparison, 1336
UICC worldwide cancer prevention project, 0003
Washington State, risk control survey, 1540
workplace programs in England in response to resolution by Trades Union Congress, 0523

SMOKING HABIT
academic health clinic patients, assessment frequency effect, 1143
addicted vs. environmentally influenced smokers, spectral analysis for assessment, 0852
adolescent males, fathers' influence, 1245
adolescent mothers in England and Wales, factors, 0517
adolescents aged 13 to 15 in Norway, 1985 survey, 0409
adolescents and adults in Australia 1983, sex differences, 0004
adolescents and adults in California, American Cancer Society survey, 0690
adolescents and adults in New Zealand, 1981 vs. 1976 rates, 0404
adolescents and young adults, predictive characteristics, 1393
adolescents, factors in initiation and cessation, 0131
adolescents, family influence vs. peer influence as factors, 1372
adolescents, hypertension, factors in etiology, 1444
adolescents in Athens, changes over 2 years, 0251
adolescents in England, survey to develop video films as educational tool, 0563
adolescents in Israel, interrelated health behaviors, 0305
adolescents in Senegal, economic, cultural, psychological factors, 0055
adolescents in Sweden, oral health relationship, 0456
adolescents in Western Australia, health education program effect, 0006
adolescents, independence from adult authority and value of education as factors, 0696
adolescents, relationship with difficult temperament in young adulthood, 1394
adolescents, respiratory symptoms relationship, 0240
adolescents, self-efficacy scale as predictor, 0851
adolescents, tar/nicotine levels and type of antismoking campaign, relationship, 0232
adolescents, value approach to cessation, reduction, prevention, 1541
adult Americans, measure of health strategies and behaviors, 1396
adults in Australia, 0008
adults in Italy, consumption trends since 1900, males vs. females, 0331
adults in Norway, cardiovascular disease risk factor screening program, 0411
adults in Norway, 10-year changes, sex differences, 0408
adults in the United States, survey of 23 States and District of Columbia, 0816
adults in United States, national sampling by Office on Smoking and Health, 0974
air crewmen, coronary artery disease risk factors, 1465
Arab and Jewish adolescents in Israel, with other health-related behaviors, 0306
army medical company personnel, effect on physical fitness testing, 1290
asbestos-exposed shipyard workers, risk relationship, 0678
asbestos-exposed workers, pleural plaque relationship, 1389
asbestos workers, factor in respiratory abnormalities, 0096
asbestos workers' morbidity and mortality, interrelationship, 0515
asbestos workers, comparison with mesothelioma patients and postal workers, 1223
asthmatic patients at age 21, followed from age 7, 0022
asthmatics, factor in reversible and fixed airway obstruction, 0511
asymptomatic middle-aged males, longitudinal study of lung function effects, 0223
athletes in various sports in Israel, training level as factor, 0316
bidi, hukka, and cigarettes as factors in pulmonary heart disease, 0275
bladder papilloma patients, cancer risk relationship, 1026
British soldiers 1959-1971, trends, 0539
cancer patients, epidemiology data system, 1269
cancer vs. general hospital employees vs. general population, 0518
changing patterns in the United States, effect on tobacco industry, 0784
children aged 10 to 12 in Australia, predictive factors, 0040
children and adolescents in Australia, sex differences, 0012
children and adolescents in Manitoba, Canada, survey for antismoking program planning, 0081
children and adolescents, predictors of change over time, 1542
children and parents, hospital drug surveillance program, 1052
children grades K-6, factors in initiation, 0779
children, longitudinal study of coronary disease risk relationship, 0959
chloromethyl ether-exposed workers, lung cancer relationship, 1388
chronic bronchitis patients, pulmonary function adaptation to ozone, 1024
chronic obstructive pulmonary disease patients, hysteresis relationship, 0679
college and university students in Nigeria, sex ratio, 0406
community vs. institution nurses, education and personality as factors, 0447
copper smelter workers, effect on lead, cadmium, and arsenic levels, 1244
coronary artery disease patients, 5-year treatment program, 1416
coronary bypass patients, diet therapy effect on arteriosclerosis, 0719
coronary bypass surgery patients, efficacy of in-hospital intervention program, 1074
coronary disease patients, blood circulation effects, 0888
coronary disease patients, effect on artery spasm incidence, 0887
coronary disease patients, effect with hostility on future events and mortality, 1305
coronary disease prevention trial participants, validity of self-reports, 0057

SUBJECT INDEX

diabetic adolescents, cardiovascular disease evaluation, 1417
diabetics, effect on retinopathy, 0239
doctors in Norway, changes between 1974 and 1984, 0410
doctors in Sudan, incidence and initiation factors, 0448
doctors, teachers, athletes, armed forces members in Egypt, sex ratio, 0173
duodenal ulcer patients, attributable risk in males vs. females, 0650
elderly persons, males vs. females, 0796
emergency medical technicians, occupational stress as factor, 1362
ethnic groups in Hawaii, cancer incidence and mortality relationship, 0833
extroverts vs. introverts, interactive effects of personality and smoking, 0567
factory workers in Japan, factor in peptic ulcer incidence, 0382
farmers in Japan, effect on serum antibodies to *Micropolyspora faeni*, 0366
head and neck cancer patients, second primary cancer risk factor, 0715
heroin addicts, buprenorphine treatment effects, 1056
high school and college students in Virginia, survey for curriculum development, 1512
high school seniors, changing consumption patterns, 1104
high school students and adults in southwest Texas, effect of intervention programs, 1481
high school students in Israel, effect of science-oriented antismoking program, 0311
high school students in Italy, alcohol consumption and drug use relationship, 0342
high school students in Italy, efficacy of program for cessation/prevention, 0336
high school students, seventh grade prevention program effect, 1131
Hispanics vs. whites, respiratory disease relationship, 1190
hospital inpatients in Connecticut, information to be included in tumor registry, 0770
hospitalized lung disease patients, relationship with occupation and residence, 0519
hypertensive patients, risk factor for stroke, 1485
Indian adults, lung function effect with socioeconomic status and diet, 0292
industrial workers, cancer incidence relationship, India, 0270
industrial workers in Ireland, 10-year followup of mortality relationship, 0303
industrial workers in Poland, laryngeal cancer risk factor, with occupational exposures, 0432
infertile males, effect on sperm quality, density, motility, 0048
inner-city junior high school students, perceived neighborhood setting as factor, 0798
ischemic heart disease patients, second event effect on cessation, with age and education, 1088
junior high school students in Wyoming, vs. smokeless tobacco use, 1561
junior/senior high school students, attitudes and behavioral correlates, 0873
leukemia patients, role in etiology, 1474
lung cancer patients, effect with sex, age, histological type, symptoms on growth rate, 0319
lung cancer patients, mortality relationship, 1172
lung cancer patients, relationship with vitamin A intake, 0832
lung cancer surgery patients, effect on short- and long-term survival, 0186
male lung cancer patients, effect on interferon induction, 0609
males at age 31, predictive factors at age 19, 0494
males vs. females in Japan, lung cancer relationship, 0349
males vs. females, motives based on adolescent personality measures, 0674
medical center inpatients, relationship with obesity, 1441
medical college students in India, related symptoms, 0263
medical students aged 19 to 25, effect on ventilatory parameters over time, 0166
medical students in England, changes from 1972 to 1981, 0558
men over 45, lung cancer screening program effectiveness, 1241
men vs. women, effect on longevity, 1402
middle-aged males in Sweden, 10-year coronary disease intervention trial effects, 0473
middle-aged males in Sweden, long-term study of disease relationship, 0472
middle-aged males vs. females, personality correlates, 0670
middle-aged men, coronary disease mortality risk factor, 0676
milk drinkers vs. nondrinkers, factor in chronic bronchitis, 1007
miners in Canada, cancer risk factor with occupational exposures, 0097
multiple myeloma patients, relationship, 1310
myocardial infarct patients, factor in rehabilitation program, 0152
myocardial infarct patients in Shanghai, risk relationship, 0147
myocardial infarct patients, long-term effects on morbidity, mortality, 0300
myodardial infarct patients, effect on platelet aggregation, 0608
noise-exposed workers, high blood pressure relationship, 1418
non-Hodgkin's lymphoma patients, risk relationship with AIDS-related factors, 1254
nurse practitioners, 0771
nurses, changing patterns and attitudes, 0773
nurses in hospital vs. college training programs, differences, 0025
nurses in Minnesota, reasons for quitting and factors in recidivism, 1124
nurses in North Carolina, attitudes and characteristics, 1326
nurses with master's degree, demographic characteristics, 1422
obstructive airways disease patients, prime risk factor, 0617
occupationally exposed workers, risk factor with alcohol consumption, 0720
ocular inflammation patients, differences, 1004
oral cancer patients, Israel compared to United States, 1282
oral cancer patients, risk factor for additional tumors, 0702
oral lesion patients, oral cancer risk, 0163
patients with Buerger's disease, effect on disease progression, 0384
patients with sexual dysfunction, relationship, 0315
physicians in Japan, mortality relationship, long-term followup, 0390
physicians, mortality relationship, 1399
physicians, personality correlates of initiation and cessation, 1308
population in rural Shanghai, hypertension relationship, 0146
pregnant adolescents, independent and dependent behavioral factors, 0657
pregnant adolescents, prenatal care effect on smoking behavior, 0658
pregnant women, birth defects association, 1043

pregnant women, effect on breast feeding practices, 0041
pregnant women, effects, 0162
pregnant women in France, trends 1972-1981, 0238
pregnant women in Norway, age, marital status, education as factors, 0418
pregnant women, low birth weight relationship, 0077
pregnant women, underestimation by heavier smokers, 0545
psychiatric patients in group therapy sessions, 1301
psychiatric patients, role in early mortality, 1095
pulmonary disease patients, 1558
school children in Dundee, Scotland, comparison with earlier studies, 0583
schoolchildren in Norway, educational plans and social network variables as factors, 0416
secondary school students, effect of transfer from elementary school, 0596
secondary school students in Australia, survey, 0005
soldiers, effect on task performance under extreme environmental conditions, 1081
staff nurses vs. student nurses vs. high school teachers, related factors, 1087
steel workers, lung cancer risk relationship, 0635
student nurses and teachers in England, changes during first year of training, 0559
students aged 12 to 18 in Utah, sex ratio of usage patterns, 1495
students aged 12 to 14, health education assembly effect on cessation, recidivism, 1042
students in Argentinian technical school, 0002
students in grades 7 through 12 in Ohio, sex ratio and changes over time, 1341
students in high schools with/without designated smoking area, effect, 0611
surgery patients, postoperative complications, relationship, 0471
teachers in primary and secondary schools in Wales, differences, 0597
twins, heredity and environment as factors, 0754
twins in Finnish cohort study, factor in morbidity and mortality at 6-year followup, 0203
university staff and students, changing ratios in men vs. women, 0208
university women students, characteristics and motivation, 0052
uranium miners, interactive effect with radon daughter exposure, 1492
uranium miners, lung cancer risk factor with radiation exposure, 1350
urban black adolescents, antecedents, 1225
urban vs. rural residents, effect on chronic bronchitis incidence, 0427
vascular surgery patients, risk relationship, 0172
Veterans Administration Medical Center employees, 0970
voluntary brand switchers, smoking pattern changes, 1016
women, effect on myocardial infarct incidence, Framingham study participants, 0987
women, health effects in oral contraceptive users, 0549
women in late pregnancy, cardiovascular effects, 0449
women in Sweden, longitudinal study of risks, 0464
women, lung cancer relationship, 0092
women, myocardial infarct risk with hypertension and oral contraceptive use, 1053
young, middle-aged, elderly men, effect on sex hormone levels, 0054
young women, need to achieve as factor, 1384
youths and adults in rural community of Nepal, sex ratio, 0393

SMOKING MACHINES
inhalation model to discriminate between different cigarettes, 0480
lip pressure and filter coverage measurements, importance in design, 0846
new model for rats developed by Tobacco and Health Research Institute, 1090
puff machine delivers variety of shapes and volumes, 1447

Smoking, marihuana *See* **MARIHUANA SMOKING**

Smoking, maternal *See* **MATERNAL SMOKING**

Smoking, parental *See* **PARENTAL SMOKING**

Smoking, passive *See* **PASSIVE SMOKING**

Smoking, paternal *See* **PATERNAL SMOKING**

Smoking, pipe *See* **PIPE SMOKING**

Smoking, reverse *See* **REVERSE SMOKING**

SMOKING SURVEYS
adolescents, validation of self-reported smoking status, 0972
Allegheny County, Pennsylvania, Health Department, smoking policy revisions, 1382
Allegheny County, Pennsylvania, smoking education in elementary and secondary schools, 1383
Athens, Greece, changes in adolescent smoking habits over 2-year period, 0251
Australia, adolescents, sex ratio and lung function correlations, 0044
Australia, factors associated with smoking in children aged 10 to 12, 0040
Australia, heart disease risk factor prevalence survey 1980, 0016
Australia, nurses trained in hospital vs. college programs, 0025
Australia, prevalence and patterns in adults 1983, 0004
Australia, "Quit For Life" antismoking campaign, efficacy, 0009
Australia, secondary school students, 0005
Australia, students in last year primary school and high school, sex differences in rates, 0012
Australian petroleum workers, cancer risk relationship, 0035
Belgium, 10-year monitoring of cardiovascular trends and determinants, 0059
Busselton (Australia), patterns compared with Sydney suburb, 0008
California, adults and adolescents, attitudes, beliefs, and behaviors, 0690
Canada, seventh grade students for evaluating peer-assisted prevention program, 0083
Canada, smoking among population subcategories, variations over time, 0061
Canada, 4-year changes in smoking rates, effect of community smoking control project, 0079
Canadian students, grades 10 through 12, 0131

SUBJECT INDEX

Centers for Disease Control behavioral risk factor surveillance survey, smoking data, 0816
Czechoslovakian plant workers, cost benefits analysis of absenteeism in smokers vs. nonsmokers, 0153
China, medical services workers, attitudes toward smoking, 0149
Current Population Survey, smoking questions in September 1985 and 1986, 0973
Egypt, doctors, teachers, athletes, armed forces members, 0173
England, medical students in Manchester, 10-year changes, 0558
ex-smokers, identification of variables associated with cessation, 1142
female college students and fathers, 1222
Finland, sex ratio of trends in smoking decline 1978-1985, 0201
Finland, university staff and students, 0208
France, respiratory symptoms and smoking among adolescents, 0240
France, trends in smoking among pregnant women 1972-1981, 0238
French adolescents, parental influence on onset of smoking, 0236
health plan participants, morbidity and mortality effects of less hazardous cigarettes, 0641
health service personnel in a cancer vs. a general hospital, 0518
high school seniors, changing patterns, 1104
high school students, problems associated with tobacco, alcohol, and marijuana use, 0648
Hispanic Health and Nutrition Survey, 0978
Hungary, consumption and filter use, lung cancer relationship, 0260
India, medical college students, 0263
Iowa junior/senior high school students, behavioral correlates, 0873
Ireland, schoolchildren in Dublin, factors related to initiation/maintenance, 0294
Ireland, social and cultural influences on smoking behavior, 0295
Israeli adolescents, interrelationship of health-related behavior and smoking, 0305
Italy, health professionals, 0335
Italy, high school students aged 15 to 18, association with alcohol consumption and drug use, 0342
Italy, temporal trends in alcohol consumption and smoking in Torin population, 0346
Japan, attitudes and viewpoints of elementary schoolchildren and older students, 0353
Japanese junior high school students, 0351
Kentucky, students, parents, teachers, effect of involvement with tobacco production on attitudes, 0957
Manitoba, Canada, schoolchildren grades 3 to 12, 0081
Minnesota, reasons for quitting and factors in recidivism among nurses, 1124
Mumbwa, Zambia, smoking habits and attitudes toward quitting, 1563
National Health and Nutrition Study, 10-year followup, 0976
National Health Interview Survey, 0979
national sampling by Office on Smoking and Health, 0974
Nepal, youths and adults in rural community, sex ratio, 0393
New Zealand, fourth cardiovascular risk factor survey of small town, 0405
New Zealand 1981 census data, comparison of smoking with 1976 rates, 0404
New Zealand, public attitudes toward restraints on smoking and cigarette promotion, 0403
Nigeria, college and university students, sex ratio, 0406
northern England, smoking patterns and background factors among children and adolescents, 0531
Norway and other European countries, social network variables as predictors of smoking, 0416
Norway, changes in smoking habits of doctors 1974 to 1984, 0410
Norway, male theologians compared with general male population, 0407
Norway, smoking habits of adolescents aged 13 to 15, 1985 survey, 0409
Norway, 10-year changes in smoking habits, males vs. females, 0408
nurses in Connecticut, 0773
Ohio, students in grades 7 through 12, changes over time, 1341
Ontario, Canada, knowledge and attitudes toward smoking restrictions, 0138
Peoples Republic of China, urban and rural areas, 0144
Perth, Australia, age and sex as factors in adult smoking rates, 0013
Scotland, children and adults in Dundee, 0583
Scotland, portable, low-cost, reliable measuring device for carbon monoxide monitoring, 0588
secondary school students, antismoking campaign effect on habits, 0235
Shanghai, China, cancer and other diseases, risk relationship, 0143
Shanghai, hypertension relationship in rural population, 0146
southwest Texas, high school students and adults, media and community interventions, 1481
students in grades 7 to 12, beliefs and attitudes, effect on initiation, 0696
Sudan, prevalence of smoking-related diseases in doctors, 0448
Switzerland, smoking initiation in women following pregnancy, 0490
televised cessation program participants, 0855
two communities compared for disease risk associated with smoking, 1477
undergraduate students in the midwest, attitudes toward and use of smokeless tobacco, 0844
United States adults 1920-1978, pancreatic cancer relationship, 1390
university hospital staff, faculty, and students, 0207
university women students, 0052
Utah junior and senior high school students, smokeless tobacco use and smoking, 1495
Wales, teachers in primary and secondary schools, differences, 0597
Western Australia, health education program effect on prevalence in adolescents, 0006
Wisconsin adults, 1551
women in New York State, cervical cancer screening program, 1255
workplace, attitudes toward restrictions, complaints of nonsmokers, 1351
Wyoming, smokeless tobacco use vs. smoking in junior high school students, 1561
young British soldiers, 1959-1971, 0539

SNUFF
buccal mucosal effects in hamsters, 1058
hamster embryo cells, cocarcinogenic effects with known carcinogens, 0412
health education and behavioral training to prevent use by adolescents, 1559
nitrosamines, carcinogenicity in rats, 0993

site-specific cancer incidence relationship, 0988
students aged 12 to 18 in Utah, sex ratio of usage patterns, 1495
sugar content, dental and periodontal disease relationship, 1405
teeth-cleaning usage in India, cancer risk relationship in women, 0269
tobacco-specific and volatile nitrosamines in Swedish samples 1981-1983, 0466
uranium concentration as risk factor for cancer in users, 0273

SNUFF-DIPPING
(*See also* SMOKING)
adolescents, oral health relationship, 0456
dental and periodontal disease relationship, 1405
high school students in Arkansas, sex ratio, 0625
neuromuscular disease relationship, 1463
periodontal disease and mucosal health, effects, 0819
women in India, cancer risk relationship, 0269

SOCIOECONOMIC STATUS
(*See also* DEMOGRAPHIC FACTORS)
air crewmen, coronary disease risk factors determination, 1465
cancer etiology, effect with smoking, 0960
cancer incidence, with smoking and alcohol consumption, 0492
cancer mortality relationship in Poland, 0433
chronic illness and absenteeism, smoking relationship, 0543
cigarette tax changes and health education, consumption effects by social class, 0542
congenital heart disease relationship, with maternal smoking and other factors, 1025
coronary disease risk relationship to educational level, 0297
depression epidemiology, effect with smoking, 0686
education and social support systems, effect on smoking habit, 1477
junior high school students, factor in smoking prevention curriculum efficacy, 1234
lung cancer incidence, risk factors with smoking, 1375
lung cancer mortality, with air pollution and smoking, 0352
lung function relationship in Indian adults, smoking and diet as factors, 0292
Mormons, cervical cancer relationship, 1491
multiple myeloma epidemiology, with smoking, 1310
population subcategories in Canada, variations in smoking over time, factor, 0061
postprimary schoolchildren in Dublin, factor in smoking initiation and maintenance, 0294
pregnancy outcome effect, with smoking, age, alcohol consumption, 0045
pregnant women, effect on outcome, 0077
respiratory illness in India, factor with air pollution, housing, nutrition, and smoking, 0293
smokers vs. nonsmokers vs. ex-smokers, 0350
smoking habit relationship in New Zealand, 0404
ulcerative colitis risk relationship, 1537
urban black adolescents, antecedents of smoking, 1225
urban, poor, elderly blacks, tobacco use relationship with perceived health status, 1175
youths and adults in rural community of Nepal, smoking habit relationship, 0393

SPERMATOZOA
(*See also* UROGENITAL SYSTEM)
male infertility, smoking relationship, 0048
nicotine and pharmacological agents, effect on sperm motility, 1454

SPUTUM
atypia detection, smoking-related in high-risk patients, 0764
atypical bronchial epithelial cells as markers for people at risk for lung cancer, 1461
histamine and leukotriene levels, smoking effect, 0181
metaplastic and dysplastic cells as evidence of epithelial process in lung cancer, 0462
mutagens from occupationally exposed workers, smokers vs. nonsmokers, 0422
rheological properties in smokers vs. nonsmokers with chronic bronchitis, 0323

Squamous cell carcinoma *See* **CARCINOMA, EPIDERMOID**

STATISTICAL ANALYSIS
(*See also* MATHEMATICAL MODELS)
lung cancer mortality, Oregon 1953-1982, risk factor analysis, 1375
mortality data for European countries, smoking as major cancer risk factor, 0244
mortality in Italy since 1955, trends in smoking-related diseases, 0331
pancreatic cancer mortality and adult smoking, relationships, 1390
tobacco price, consumption, product weight, trends, 0080

STEROIDS
(*See also* ADRENAL HORMONES)
placental metabolism, cigarette smoking effect, 0211
testicular androgens, pubertal, smoking and dioxin effects, 1186

STOMACH
(*See also* GASTROINTESTINAL SYSTEM)
nocturnal gastric secretion, smoking effect on inhibition, 0580

STOMACH NEOPLASMS
(*See also* GASTROINTESTINAL NEOPLASMS)
nutrition, occupation, residence, and smoking as risk factors, 0960

Stomach ulcer *See* **PEPTIC ULCER**

STRESS
auditory noise effect on task performance, smoking vs. nonsmoking condition, 0484
biochemical defense mechanisms in smoke-exposed rats, effect, 0889
cardiac, autoregulation as response, smoking relationship, 1412
cessation os smoking relationship, 0109
coffee and tea consumption, effect with smoking and alcohol consumption, 0134
consumption level and nicotine preference effects, 0736
coping strategies as part of community antismoking program, efficacy in southwest Texas, 1481
coping strategies needed by ex-smokers, 1142
discomfort in smoking-permitted vs. smoking-restricted offices, smokers vs. nonsmokers, 0099

electric shock treatment in monkeys, smoking as avoidance behavior, 0356
emergency medical technicians, effect on alcohol consumption and smoking, 1362
Healthstyles program to promote health-enhancing behavior, 0074
inoperable cancer patients, treatment approach, 0785
job performance and health effects, 1442
Kaiser-Permanente risk reduction program, self-help vs. group sessions, 0642
microcomputer program for reduction, 1075
modifiers and manifestations in black and white household populations, 1265
motor task performance by smokers, effect with personality, 0530
nicotine effect on stress-related responses in rabbits, 1021
nicotine-seeking behavior, correlates with/without stress, 0694
nicotine utilization for reduction in light vs. deep inhalers, 0483
noise reactivity, effect of mental stress, physical activity, and smoking, 0486
Normative Aging Study in middle-aged men, longitudinal effects, 1046
nurses, smoking habit relationship, 1087
pregnant adolescents, perception as factor in substance use, 0657
pregnant women, effect with nutrition and smoking on infant birth weight, 0555
psychosocial stress as factor in maintaining tobacco habit, 1066
puffing and inhalation patterns, effect of different levels of stress, 0481
recidivism factor at 12-month followup, 0655
sedative vs. stimulant smokers, perceived stress and arousal as factors in behavior, 0561
substance-abusing families, prevention/intervention services for children, 1493
worksite, effect on smoking cessation programs, 1432

STUDENTS
aged 11, 13, and 15 in Norway, education and social network as smoking factors, 0416
college and university in Nigeria, smoking habits, 0406
college, factors influencing abstinence in self-quitters of smoking, 1272
college, health center physician's advice to quit smoking, effect, 1283
college undergraduates in the midwest, attitudes toward and use of smokeless tobacco, 0844
elementary and junior high school in California, education program for smoking prevention, 0675
female nurses and teachers in England, changes in smoking habits during training, 0559
fifth and sixth grade, intervention program effectiveness in preventing smoking, 1103
fifth to seventh grade, mass media and school health education for smoking prevention, 1503
grades 7 through 12 in Western Australia, health education effect on smoking, 0006
grades 3 to 10 in Washington State, prevention of smoking curriculum, long-term followup, 1516
health education for 12- to 16-year-olds in North Karelia to prevent smoking, 0200
high-risk sixth graders, smoking prevention curriculum, effect of booster sessions, 1532
high school, administrative problems related to alcohol and marijuana use and smoking, 0648
high school and college in Virginia, cardiovascular knowledge assessment, 1512
high school, designated smoking area effect on smoking incidence, 0611
high school, effect of seventh grade antismoking program on smoking prevalence, 1131
high school, health education for smoking cessation/prevention in Italy, 0336
high school in southwest Texas, effect of intervention programs on smoking habits, 1481
high school, leaders of antismoking program for fourth graders, 1217
high school students in Israel, smoking prevention program effectiveness, 0311
high school, tar/nicotine levels consumed and type of antismoking campaign, relationship, 0232
inner-city junior high school, perceived neighborhood setting as factor in drug use, 0798
Japanese junior high school, smoking habits compared to U.S. data, 0351
junior and senior high school, tobacco chewing effect on smoking initiation, 1373
junior high school, classroom television smoking prevention program, efficacy, 0724
junior/senior high school, behavioral correlates of smoking, school and peers as factors, 0873
lung function changes in vocational school smokers, 0188
medical college students in India, smoking prevalence, 0263
medical in England, changes in smoking knowledge, behavior, opinions 1972-1981, 0558
prevention of smoking curriculum, efficacy of maximum vs. minimum teacher support, 1235
prevention/reduction of smoking in adolescents, value approach, 1541
school-based smoking prevention program, skills training and health information for coping, 1550
secondary school, effect of transfer from elementary school on smoking habits, 0596
seventh grade, classroom and television smoking prevention program, efficacy, 0725
seventh grade in Canada, peer-assisted smoking prevention program, 0083
seventh grade, parental involvement in drug abuse prevention program, effect on intentions, 0726
sixth and seventh grade, social-psychological intervention, effect on smoking initiation, 1062
technical school in Argentina, survey of smoking attitudes, 0002
12- to 14-year-olds, health education assembly effect on smoking cessation, 1042
university, changing smoking behavior in male vs. female students, 0208
university women, smoking characteristics and motivation, 0052

SUBJECT INDEX

Substitutes, tobacco *See* **TOBACCO SUBSTITUTES**

Sugar content *See* **CARBOHYDRATE CONTENT**

Sugars *See* **CARBOHYDRATES**

SULFUR COMPOUNDS
- aldehydes in cigarette smoke, protective effect in rats, 1428

SULFUR DIOXIDE
- respiratory effects in exposed workers, smoking role, 1061

TAR CONTENT
- (*See also* AROMATIC HYDROCARBON CONTENT)
- agricultural methods of increasing leaf nicotine content, effects, 0926
- biochemical effects of reducing tar yield of cigarettes, 0533
- British cigarettes, changing levels, 0527
- burley tobacco, genetic variability to reduce levels, 0911
- cigarette preference relationship, with sweet-bitter taste dimension, 0795
- cigarettes from developing countries, WHO-sponsored analysis, 0496
- cigarettes in western Scotland, relationship with lung cancer mortality, 0590
- domestic and imported cigarettes in Australia, 0007
- Egyptian cigarettes, reduction following legislation, 0173
- Italian cigarettes, 0331
- lung cancer risk relationship, 0050
- myocardial infarct survival relationship, international study, 0547
- reduced levels, effect on bronchial epithelium of smokers, 1177
- short-term thermal treatment system for tobacco expansion, reduction effect, 0442

TAR REDUCTION
- genetic method in tobacco growing, 1331
- lung cancer risk effect, 1216

TARS, CIGARETTE
- (*See also* AROMATIC HYDROCARBONS)
- activation/deactivation of mutagens by human lung preparations, 0337
- arachidonic acid metabolism in human monocytes, effect of benzo(*a*)pyrene, 0488
- bronchial cancer formation in hamsters, carbon filter effect, 0175
- co-mutagenic activity with norharman, 0395
- DNA single-strand breaks, effect, 0178
- enzyme activities in rat lung and liver, effect, 0343
- hamster embryo cells, cocarcinogenic effects with known carcinogens, 0412
- 7H-dibenzo(*c, g*)carbazole, polynucleotides and DNA binding, 1359
- hypnosis in reduction of intake, effectiveness, 1325
- keratins, expression in vitro, effect of tobacco smoke components, 0157
- lung deposition during smoking, role in emphysema etiology, 0136
- lungs and liver of rats pretreated with N-acetylcysteine, mutagenicity, 0339
- mutagenic and carcinogenic compounds in Indian cigarettes, 0266
- mutagenicity of particulate phase of environmental tobacco smoke, 0195
- radicals, toxicity, 0961
- radon decay products on smoke tar particles, bronchial deposition, 0752
- riboflavin, chlorophyllin, chlorophyll, antimutagenic activity, 0394
- size distribution of cigarette smoke particulates, 0624

TARS, TOBACCO
- aging effects on smoke nicotine and particulates content, 0267
- carbon and nitrogen content of leaf, effects, 0921
- cell wall and soluble cell fractions, particulates contribution, 0922
- mutagenic and carcinogenic compounds in Indian tobacco products, 0266
- reduction by selection and breeding, 1330

TASTE
- cigarettes, discrimination of own brand by smokers, 0795
- conditioned aversion in rats, nicotine effect, 0521
- nicotine self-administration in rats, taste aversion effect, 0909
- secondary reinforcer of smoking behavior, salience in maintenance and satisfaction, 0693

TAXATION
- (*See also* LEGISLATION)
- changes in taxes and health education, consumption effects by social class, 0542
- future effect on tobacco industry as seen by U.S. Department of Agriculture, 0784
- quarterly publication, issues affecting the tobacco industry, 1270
- tobacco industry, estimated effects, 1319

TEETH
- (*See also* DENTAL DISEASES; PERIODONTAL DISEASES)
- dental hygiene as cancer risk factor, 1520
- plaque formation, gingival vascular response in smokers vs. nonsmokers, 0455
- plaque formation in cigarette vs. cigar vs. pipe smokers vs. nonsmokers, 1097

TERATOGENESIS
- (*See also* BIRTH DEFECTS)
- tobacco alkaloid effects, 1494

TERPENOIDS
- biosynthetic aspects in tobacco, 0923
- blue mold effects on tobacco constituents, 0930
- tobacco type and curing methods effects, 0924
- virus infection effects, 0931

TESTES
- (*See also* UROGENITAL SYSTEM)
- androgen hydroxylase activity, effects of puberty, smoking, and dioxin, 1186

THIOCYANATES
- (*See also* CYANIDES)
- blood levels, cigarette yield, smoking history, and smoking behavior as determinants, 0905
- cessation of smoking effect, 0119

- maternal serum and cord blood levels in pregnant smokers vs. nonsmokers, 0213
- passive smokers vs. smokers vs. nonsmokers, 0194
- plasma level as predictor of theophylline clearance, 0834
- pregnant women, concentrations in smokers vs. passive smokers vs. nonsmokers, 1471
- self-reported smoking behavior in coronary disease prevention trial, validity confirmed, 0057
- serum and saliva levels as smoking status indicators, 0219
- serum and urine levels as smoking status determinant, 0215
- umbilical cord levels, maternal smoking effects, 0423
- urine levels in smokers vs. nonsmokers, 0375

THROMBOANGIITIS OBLITERANS
(*See also* ARTERIAL DISEASES)
- Buerger's disease patients, smoking effect on disease progression, 0384
- cell-mediated immunity against tobacco antigens in patients, 0274

THROMBOSIS
(*See also* VASCULAR DISEASES)
- coronary arteries, smoking effect, 1554
- thromboxane and prostacyclin production and smoke exposure effects, 0918

Thrombosis, coronary *See* **CORONARY DISEASE**

TOBACCO
(*See also* CHEWING TOBACCO; SNUFF)
- analytical studies in tobacco carcinogenesis, assay methods, 1211
- antidrug education, message source credibility determination, 0860
- arsenic and tobacco mosaic virus levels, comparison of Western and Chinese brands, 0185
- chemical and physical factors of leaf, altering to improve safety, 1329
- chemical composition of experimental varieties, determining factors, 0823
- chemical precursors that form hazardous constituents in smoke, 0898
- chutta tobacco from India, levels of nicotine, reducing sugars, chloride, total nitrogen, 0278
- consumption in tobacco-growing states, crop size relationship, 0956
- consumption patterns in Greece, effect of health education and legislation, 0253
- experimental tobacco carcinogenesis, project overview, 1207
- hallucinogenic and narcotic agent in pre-Columbian Aztec culture, 0400
- N-nitrosodiethanolamine levels in tobacco products, 1197
- origins and use among aboriginal cultures, 0085
- quality and composition, near infrared spectroscopy for measurement, 1318
- quantitative correlation of lifetime consumption with development of various diseases, 1037
- selenium, cadmium, beryllium content, biological implications, 0751
- soil-borne diseases, control methods, 0824
- Turkish, trace elements in cigarette vs. pipe tobacco, 0499

TOBACCO ADDITIVES
- mutagenicity and carcinogenicity in low-tar cigarettes, 1198
- smoke-absorbing material to reduce levels of cigarette smoke, 0864
- Turkish pipe tobacco, effect on trace elements vs. cigarette tobacco, 0499

TOBACCO AGING
- reduction of hazardous compounds in leaf and smoke, 0881
- smoke nicotine and particulates content, 0267

Tobacco alkaloids *See* **ALKALOIDS, TOBACCO**

Tobacco amblyopia *See* **AMBLYOPIA, TOBACCO**

TOBACCO AROMA
- chemical evaluation, 1330

TOBACCO CHEWING
- adolescents, periodontal alterations, relationship, 0756
- buccal mucosa cells and circulating blood cells, effect, 1489
- college undergraduates in the midwest, attitudes toward and use of smokeless tobacco, 0844
- dental and periodontal disease relationship, 1405
- diabetic retinopathy risk factor, 0284
- high school students in Arkansas, sex ratio, 0625
- junior high school students in Wyoming, sex ratio vs. smoking, 1561
- mortality rates compared with rates for other forms of withbacco use, 0289
- mortality reduction in users who quit or reduce use, 0287
- mortality risk factor determination, 0290
- neuromuscular disease relationship, 1463
- oral and pharyngeal cancer, risk relationship, 0424
- oral cancer risk relationship, 0272
- pancreatic, bile-duct, and gallbladder cancer risk relationship, 0246
- periodontal disease and mucosal health, effects, 0819
- serum high density lipoprotein cholesterol, quantity consumed as factor, 0285
- site-specific cancer incidence relationship, 0988
- students in junior and senior high school, effect on smoking initiation, 1373
- women in rural India, long-term effect of intervention strategies, 0291

TOBACCO CONTAMINANTS
(*See also* PESTICIDES)
- dinitroaniline herbicide activity in soil and plant tissues, 0927
- maleic hydrazide, control with growth regulators, 1292
- pesticide control engineering, 1328
- pesticide residue reduction, breeding methods, 1556
- plutonium aerosols on tobacco grown near chemical plant, potential dose, 1443

TOBACCO CURING
(*See also* AGRICULTURAL PRACTICES)
- burley, for quality control, economy, and smoke component yield reduction, 0884
- carcinogenicity of conventionally cured and homogenized leaf cured tobacco, 0603
- chemical composition of tobacco, effect, 0823
- enzyme activity in leaf components during air curing, 0891

hazardous leaf components, method for reduction/elmination, 1329
leaf chemical composition changes and moisture diffusion, 0925
microbial nitrate reduction and nitrite production, 0951
microorganism alteration of leaf components, chemical means, 0947
nitrate removal, procedure, 1035
pesticide residues after curing and in tobacco smoke, 1317
protein extraction, leaf, 0949
pyrolysis products effects, 0806
reduction of hazardous compounds in leaf and smoke, 0881
terpenoid fraction effects, 0924

TOBACCO EXTRACTS
estrogen production of placental aromatase in rats, inhibitory effect, 1240
immunogenicity and allergenicity in sensitive vs. nonsensitive subjects, 0966
mucosa of hamster cheek pouch, ultrastructural and histological effects, 0498
oral microorganisms implicated in periodontal diseases, smokeless tobacco extracts effect, 1029

TOBACCO FLAVOR
chemical evaluation, 1330
mutagenicity and carcinogenicity of additives in low-tar cigarettes, 1198

TOBACCO INDUSTRY
(*See also* COST BENEFITS ANALYSIS, ECONOMICS)
advertising, health claims and images, *Time* magazine 1944-1983, 0845
American cigarette industry, public policy and political economy, alternatives, 0789
British, tar, carbon monoxide, and nicotine content of cigarettes, 0527
Canada, advertising expenditures vs. antismoking articles in women's magazines, 0090
cigarette advertising ban, effect on tobacco companies' market shares, 0776
current outlook by U.S. Department of Agriculture, 0784
Italy, trends in sales and consumption since 1900, 0331
Latin America, denationalization and dynamics of international cigarette oligopoly, 0790
liability in cigarette-induced fires, 0843
New Zealand, sports sponsorship and cigarette advertising, public attitudes, 0403
newspaper advertising in Western Australia during parliamentary debate on smoking, 0020
quarterly publication of variables affecting the industry, 1270
societal benefits and cost/risks of smoking, 0128
students, parents, teachers, effect of involvement on smoking-related attitudes, 0957
supply and demand, taxes, policy changes, estimated effects, 1319

TOBACCO LEAF COMPONENTS
burley curing method, effects, 0884
cadmium, potential for reduction, 0916
carbon/nitrogen ratio effects, 0921
carotenes, degradation products and oxygen and ultraviolet light exposure effects, 0929
chemical constituents, effect of enzyme activity during air curing, 0891
chemicals, methods for reduction/elimination, 1329
compositional changes and moisture diffusion during curing, 0925
essential oils, lipids, fatty acids, carbonyls, and phenolic substances in lanka tobacco, 0268
genetic manipulation to reduce proteins, 1032
health-related compounds, chemical analysis, 0950
lung damage from toxins also found in cotton dust, 1309
metals in tobacco grown on sludge-amended soil, 1030
microorganism alteration, chemical means, 0947
moisture content during storage, effects, 0952
nicotine in allergenic extracts by high performance liquid chromatography, 0217
nitrate, removal procedure, 1035
nitrogen and chloride fertilizer effects, 0920
pesticides, chemical composition effects, 0948
plutonium in tobacco grown near chemical plant, potential dose, 1443
polyphenols and catechol, genetics and breeding, 1321
precursors of hazardous tobacco smoke compounds, determination, 0821
protein extraction techniques, 0949
safety improvement by genetic alteration, 1033
tobacco mosaic virus in disease etiology, 0151
virus infection effects, 0931

TOBACCO MOSAIC VIRUS
(*See also* VIRUSES)
mechanisms of infection, 0931
neoplasia development in smokers, role in etiology, 0151
Western vs. Chinese brands, levels, 0185

TOBACCO PROCESSING
aging effects on smoke nicotine and particulates content, 0267
burley, mycotoxin formation prevention equipment, 0882
lipid reduction effects, 0804
moisture content during storage, 0952
reduction of hazardous smoke constituents, techniques, 0898
short-term thermal treatment system for expansion, 0442

TOBACCO PYROLYSIS PRODUCTS
alpha radioactivity of filtrates, potential for lung damage, 0865
benzo(*a*)pyrene monooxygenase activity in rat lung, effect with alcohol consumption, 1293
burley curing method, effects, 0884
field spraying with trace elements, effect on smoke content, 1311
mutagenic condensates in African tobaccos, 0445
N-nitrosodiethanolamine levels in tobacco products, 1197
pesticide residues in cured tobacco and smoke, 1317
1-phenylcyclohexene, toxicological evaluation and interaction with phencyclidine, 1340
polonium-210, distribution and clearance of radioactivity in rat lung, 1261
precursors and modes of formation, 0806

SUBJECT INDEX

sidestream smoke carcinogens, report on selected methods of analysis, 0250
sidestream vs. mainstream smoke, carcinogenicity in hamsters, 1209
tar from burley tobacco, genetic variability to reduce levels, 0911
Turkish cigarette vs. pipe tobacco, trace elements, 0499

TOBACCO, RECONSTITUTED
structural alterations to reduce smoke component yields, 0928

TOBACCO SMOKE
(*See also* CIGARETTE SMOKE; SMOKING)
aldehydes, protective effect of sulfur compounds and naturally occurring metabolites, 1428
alkylamines and alkylthiols in polluted air, chromatographic determination method, 0362
atherosclerotic lesions, etiologic relationship, 1526
carcinogens, inhibition by alcohols of localization in tumor sites, 0936
chemical/biological analysis of smoke condensate, 1320
chemicals recognized by IgG antibodies in human sera, 0028
chromosomal damage by tobacco smoke components, 0488
d-nicotine levels to measure degree of racemization of l-nicotine, 0760
field spraying with trace elements, effect on content, 1311
guanylate cyclase turnover effects, 0740
hazardous constituents, identification of chemical precursors, 0898
irritant level in smokers vs. nonsmokers, 0766
lung deposition sites of smoke constituents, 0506
lung disease etiologic relationship, 0753
N-nitrosodiethanolamine levels in tobacco products, 1197
pyrolysis products related to flavor, aroma, and biological properties, 0806
ventilation in rooms, effective method, 0372
ventilatory response to hypoxia, hypercapnia, acute exposure effects, 0365
volatile and particulate phases, analysis of toxic and tumorigenic constituents, 0822

Tobacco smoke, gaseous phase *See* GAS PHASE, TOBACCO SMOKE

Tobacco smoke, particulate phase *See* TARS, TOBACCO

TOBACCO SUBSTITUTES
addictive smoking identification and nicotine gum in cessation, 0683
cardiovascular effects of nicotine gum vs. high- and low-nicotine cigarettes, 0681
nicotine chewing gum, dose requirements for smoking cessation, 1355
nicotine chewing gum, education program on use for residents in family medicine, 0761
nicotine chewing gum, effect on smoking withdrawal symptoms, 0663
nicotine chewing gum, efficacy in treatment of ulcerative colitis, 1239
nicotine chewing gum, factors affecting self-administration, 1126
nicotine chewing gum for smoking cessation, efficacy, 0027 0614 1099
nicotine chewing gum, periodontal disease risk relationship, 1348
nicotine chewing gum to prevent recidivism, 0659
nicotine chewing gum, symptoms of intolerance in smokers, nonsmokers, and ex-smokers, 0632
nicotine chewing gum to relieve withdrawal symptoms, 0522
nicotine plasma levels with nicotine gum, 0629
plastic cigarette in smoking cessation program for middle-aged men, efficacy, 0154

TOBACCO TASTE
filter for low-tar cigarettes that retains rich taste, 0383

TOBACCO VARIETIES
blond/black, filtered/unfiltered, effect on cancer etiology, 0344
blond vs. black as factors in laryngeal cancer etiology, 0347
bright, burley, Turkish, domestic Japanese, component distribution ratio, 0374
bright vs. burley, carcinogenicity, 1238
burley, genetic variability to reduce tar levels, 0911
burley, moisture content during storage, 0952
cadmium content in leaf and roots, potential for reduction, 0916
chutta tobacco from southeast India, tobacco and smoke components, 0278
cross-breeding of burley with Maryland cultivar for low-alkaloid level strain, 1028
Cuban dark tobacco, lung cancer relationship in users, 0985
flue-cured, chemical analysis of experimental tobacco, 0823
flue-cured, nitrogen fertilization, sucker control, cross-breeding effects, 0826
hazardous compound levels and disease and insect resistance, analysis, 0821
home-grown African tobacco, effect on etiology of esophageal cancer, 0445
lanka tobacco of India, chemical composition of leaf and smoke, 0268
light vs. dark tobaccos, lung cancer risk relationship, 0228
smokeless, effect of extracts on microorganisms in periodontal disease, 1029
tabtoxin resistance, recombinant DNA techniques in tobacco, 0901
terpenoid fraction effects, 0924
Turkish with very high nicotine/moderate tar delivery for less hazardous cigarettes, 1447

TRACHEA
(*See also* RESPIRATORY SYSTEM)
bacterial adherence in cells of chronic lung disease patients, smoking effect, 1249
ciliated cells from rabbits, mixed-function oxidase activity, 1316
hydrocarbons, injections as lung cancer inducers in mice, 0717
tobacco-related carcinogens, alcohol consumption effect on metabolism, 1347

TRACHEAL NEOPLASMS
(*See also* RESPIRATORY TRACT NEOPLASMS)
uranium miners exposed to radon-222, risk with smoking, 0097

TRIGLYCERIDES
(*See also* FATTY ACIDS; LIPIDS)
atherosclerosis patients with renal failure, risk relationship, 1534

cessation of smoking effect, 0119
Normative Aging Study in middle-aged men, risk factor for coronary disease, 1046

Trypsin inhibitors *See* ANTITRYPSIN LEVELS

TUBERCULOSIS
(*See also* RESPIRATORY TRACT INFECTIONS)
lung cancer risk with smoking in patients given isoniazid, 0508

Tumors *See* NEOPLASMS

Tumorigenesis *See* CARCINOGENESIS

Tumor promoting agents *See* COCARCINOGENS

Tumor initiating agents *See* CARCINOGENS

TWINS
coronary and all cause mortality in Finnish cohort study, smoking as factor, 0203
heredity and environment as factors in drug use, 0754
ventilatory response to hypoxia, hypercapnia, smokers vs. nonsmokers, 0365

Ulcer, peptic *See* PEPTIC ULCER

URANIUM
(*See also* METALS, METAL ISOTOPES)
cancer mortality in miners, radon exposure and smoking as factors, 0242
miners, radon daughter exposures and smoking, effect on lung cancer incidence, 1189
snuff levels as risk factor for cancer in users, 0273

URINE
cadmium and arsenic levels in copper smelter workers, smoking effect, 1244
cadmium and lead levels in population with low exposure, smoking effect, 0056
cadmium levels in smokers and nonsmokers, 1298
conjugate levels, diet, drugs, and smoking effect, 1510
cotinine levels in nonsmokers as measurement of smoke exposure, 0380
cotinine levels in nonsmokers, passive smoking relationship, 0245
cotinine levels in smokers who switch from high- to low-tar cigarettes, 0533
cotinine, nicotine, thioether concentrations as smoking status determinants, 0215
D-glucaric acid excretion, age, sex, smoking as factors, 0340
desmosine levels as an indicator of pulmonary elastolysis, 1147
determination of N-nitrosamines, 1404
industrial workers, smoking effect on carcinogen levels, 0402
mutagenicity in passive smokers vs. smokers vs. nonsmokers, 0194
mutagenicity in railroad workers, smoking effect, 0677
mutagenicity in smokers and cirrhotics, 0857
nicotine concentrations in rats, in study of biochemical defense mechanisms, 0889
nicotine, cotinine, and other constituents as indicators of oral cancer risk, 1184
nicotine, cotinine, hydroxyproline levels, smoking habit relationship, 0375
nicotine levels, effect of renal function impairmant, 1433
platelet activating factor levels in smokers vs. nonsmokers, 0047
prostacyclin and thromboxane levels in chronic smokers, nicotine level effect, 0668

UROGENITAL NEOPLASMS
(*See also* BLADDER NEOPLASMS; GYNECOLOGIC NEOPLASMS; KIDNEY NEOPLASMS; PROSTATIC NEOPLASMS)
Depo-Provera use in patients in Costa Rica, smoking as factor, 0811
etiological risk factors with smoking, 0344
smoking-related risk, 0812
vitamins, coffee, occupation, smoking as risk factors in Japanese, 0829

UROGENITAL SYSTEM
(*See also* BLADDER; KIDNEYS; PROSTATE; SPERMATOZOA; TESTES)
cervical fluid in premenopausal women, mutagenicity, smoking as factor, 0711
drug use, coffee consumption, smoking effect on reproductive function in women, 0626
fertility reduction in smokers, 0227
gonadal correlates of smoking, 1098
low penile systolic blood pressure, arterial disease risk, 0765
male infertility, smoking relationship, 0592
semen quality in infertile males, smoking relationship, 0048

UTERINE NEOPLASMS
(*See also* GYNECOLOGIC NEOPLASMS)
cervical cancer in women in Milan, smoking as risk factor, 0332
cervical cancer, smoking habit relationship, 0189
smoking-related risk, 0812

UTERUS
cervical dysplasia, sexual behavior and smoking as factors, 0124
nicotine effect on function in rats, 1111

Vaginal neoplasms *See* GYNECOLOGIC NEOPLASMS

VASCULAR DISEASES
(*See also* ARTERIAL DISEASES; CARDIOVASCULAR DISEASES)
abdominal aortic aneurysm, smoking role in etiology, 0631
aneurysm patients, leukocyte elastolytic activity in smokers, 0630
cigarette smoke condensate mutagenicity, 1522
MONICA project, West Germany, monitoring of trends and determinants, 0176
pathophysiologic factors in pulmonary artery morphologic changes, 1138
peripheral vascular disease patients, intervention program effectiveness, 1294
sexual arousal in patients, smoking effects, 1440
smoking effect, 0954

Ventilatory function tests *See* **RESPIRATORY FUNCTION TESTS**

VIRUSES
- (*See also* TOBACCO MOSAIC VIRUS)
- adenovirus types 5 and 7, in vitro smoke effects, 1169
- disease resistance in tobacco, breeding methods, 0883
- fibroblasts transformation, lung cancer susceptibility diagnosis, feasibility, 0800
- hepatitis B infection, liver cancer risk relationship, with smoking, 0732
- *Herpes simplex*, acyclovir and monoglyceride effects in smokers vs. nonsmokers, 1424
- infection effects on tobacco leaf components, 0931
- Nebraska Laboratory Cancer Research Center, objectives, 1154
- respiratory syncytial virus infection in infants, long-term effects, parental smoking role, 1287
- tobacco leaf infection and health related leaf component, 0933

Vision *See* **EYES**

Vital capacity measurements *See* **RESPIRATORY FUNCTION TESTS**

VITAMIN A
- benzo(*a*)pyrene-induced respiratory cancer, effect in hamsters, 0396
- beta-carotene for prevention of oral lesions and carcinomas in reverse smokers, 0065
- cancer mortality in male MRFIT cohort, risk relationship, 1130
- chronic bronchitis in milk drinkers vs. nondrinkers, smoking as factor, 1007
- dietary intake as factor in lung cancer, with smoking, 0832
- epithelial cell neoplastic progression, phenotypic analysis of arrest or reversal, 1507
- lung cancer in middle-aged men, risk relationship, 1480
- lung cancer prevention therapy in high-risk smokers, pilot study, 1517
- lung cancer relationship, with smoking and occupational exposure, 1172
- lung cancer risk relationship in women, with smoking, 0730
- urothelial cancer risk relationship in Japanese, with smoking, 0829

VITAMIN B
- $B_{12}$and folate deficiency in smokers, cancer relationship, 0606
- cancer prevention in asbestos-exposed workers with lung disease, efficacy, 1531
- lung cancer prevention, role of beta-carotene, U.S.-Finnish trial in smokers, 0986

VITAMIN C
- acute smoking effects relationship, 0604
- chronic airflow limitation relationship to blood levels in smokers vs. nonsmokers, 0125
- dietary intake effects in smoke-exposed hamsters, 0367
- formation and destruction of nitrosamines, role, 1404
- urothelial cancer risk relationship in Japanese, with smoking, 0829

VITAMIN E
- buccal pouch tumors in hamsters, anticarcinogenic activity, 1059
- lung cancer prevention, U.S.-Finnish trial, 0986
- plasma levels in smoke-exposed macaques and controls, 1446
- serum level, smoking relationship, 0578

VITAMINS
- beta-carotene and retinol deficiency in buccal mucosa of heavy smokers and alcohol consumers, 0066
- beta-carotene and vitamin A in lung cancer prevention trial in high-risk smokers, 1517
- cancer mortality in male MRFIT cohort, risk relationship, 1130
- cancer risk relationship, prospective study in New York State, interaction with smoking, 1273
- lung cancer risk reduction, dietary carotene as factor, interactive effect with tobacco, 1276
- lung cancer risk relationship in women, 0326
- serum levels, smoking relationship, 1001

Water content *See* **MOISTURE CONTENT**

WITHDRAWAL CLINICS
- effectiveness in patients with smoking-related medical conditions, 1300
- 5-day plans, success rates and criticisms, 0207
- hospital employees, 0968
- positive vs. neutral feedback and cessation vs. reduction as goals, 1336
- social skills training for relapse prevention, efficacy, 0794
- stress and probability of success in participants, 1535
- three-stage program for smoking reduction, 1149
- two-phase clinic using persuasive message and self-control, 0741

WITHDRAWAL SYMPTOMS
- cessation of smoking, reason for dropping out of program, 0209
- chronic nicotine administration in rats, detection of subjective symptoms, 1468
- clonidine effects on craving, 1488
- electrophysiological changes during long-term withdrawal, 0324
- everyday stress, increased importance and as factor in relapse, 0799
- gradual vs. abrupt cessation, effect on treatment outcome, 1118
- lateral cerebral asymmetry as cause, 0744
- nicotine chewing gum, randomized trial, 0129
- nicotine gum in cessation for addicted smokers, effect, 0683
- nicotine vs. placebo chewing gum, effectiveness, 0663
- obesity, causes, 0463
- psychomotor task response inhibition during smoking deprivation, 1136
- relaxation therapy, three-stage smoking reduction program, 1149
- sex-related differences, 0655
- sleep disturbances, respiratory problems, mouth ulcers, 0026

WOMEN
- (*See also* SEX RATIO)
- achievement motivation in young women, smoking habit relationship, 1384
- adolescent mothers, smoking habits in England and Wales, 0517

SUBJECT INDEX

age, marital status, education effect on smoking habits of pregnant women in Norway, 0418
aging, menopause, and smoking, interrelationships, 0750
alcohol consumption and smoking during pregnancy, fetal and neonatal effects, 0237
alcohol, nicotine, marijuana use before and during pregnancy in Canada, trends, 0072
anal cancer, etiologic factors, 0879
anovulatory cycles in smokers vs. nonsmokers, 1098
breast cancer detection, value of screening with/without mammography, 0123
breast cancer patients, smoking and hair dye use as risk factors, 0341
cancer and cardiovascular disease, prospective study of risk factors, 1078
cancer incidence and mortality, prospective study in Norway, 0417
cardiovascular disease and cancer mortality, smoking relationship, 1000
cardiovascular disease risk factors and interrelationships in nurses, 1054
cervical cancer, smoking as risk factor, 0189
cervical dysplasia, sex behavior, oral contraceptive use, smoking in epidemiology, 0124
cervical fluid in premenopausal women, smoking as factor in mutagenicity, 0711
cessation of smoking during pregnancy, efficacy of self-help home correspondence program, 0646
coffee, alcohol, cigarettes, marijuana use during pregnancy, fetal effects, 1262
community reproductive care program, efficacy, 0077
Depo-Provera use in women with breast or cervical cancer, smoking as factor, 0811
diabetics, red cell oxygen transport and release during pregnancy, smokers vs. nonsmokers, 0156
diet, alcohol use, and smoking during pregnancy, effects on infant growth and lactation, 1525
diet and smoking as risk factors for lung cancer, 0326
fibrinolytic activity of vein walls in oral contraceptive users, smoking effect, 0450
hematological effects of diet and smoking in the elderly, 0885
high density lipoprotein levels, effect of exercise, alcohol consumption, smoking, 0934
initiation of smoking after pregnancy, possible reasons, 0490
interagency smoking cessation program for pregnant women, 0634
longitudinal study, 12-year followup, health effects of smoking, 0464
lung cancer patients, smoking relationship, 0090
lung cancer risk factors, 0142
mastectomy patients, secondary tumors and mortality, radiation and other factors, 1067
maternal smoking effect on fetal growth, mechanism, 0379
metallic mercury exposure effects on reproductive system, 0086
Mormons, cervical cancer incidence, 1491
mortality and morbidity in women married to smokers vs. ex-smokers vs. nonsmokers, 0701
myocardial infarct in smokers vs. nonsmokers, Framingham study participants, 0987
myocardial infarct incidence, smoking and other risk factors, 1053
myocardial infarct risk in smokers under age 50, 1039
neighborhood clinic intervention program for smoking cessation during pregnancy, 0713
oral contraceptive use and smoking effects, 0321
passive and active smoking as risk factors for chronic obstructive lung disease, 0255
personality correlates in long-term smokers vs. nonsmokers vs. ex-smokers, 0670
pregnant, cardiovascular effects of smoking, 0449
reproductive functions, effect of drug use, coffee consumption, smoking, 0626
sexual arousal and smoking relationship, 1439
small-for-date infants, risk factors with smoking, 0610
smoking habits during pregnancy in France, trends 1972-1981, 0238
smoking habits in Australia, 0004
smoking patterns before, during and 1 year after pregnancy, changes, 0073
smoking-related respiratory symptoms, incidence, 0234
snuff use for teeth-cleaning and inhalation in India, cancer risk relationship, 0269
student nurses and teachers in England, stereotypic view of smokers and nonsmokers, 0559
tobacco chewing in rural India, long-term effect of intervention strategies, 0291
underestimation of smoking by heavier smokers during pregnancy, 0545
university students, smoking characteristics and motivation, 0052
urinary cotinine levels in nonsmokers, passive smoke exposure relationship, 0245
wives of smokers, passive smoking and chronic respiratory disease relationship, 0280
wives of smokers, passive smoking as cancer risk factor, 0254
worksite self-help program for smoking cessation, cost effectiveness, 1431

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